A COMPREHENSIVE STUDY OF PATIENTS ADMITTED WITH SNAKEBITE IN TIRUNELVELI MEDICAL COLLEGE HOSPITAL

DISSERTATION SUBMITTED

In partial fulfillment of the requirement for the degree of

(Branch-I)M. D. (GENERAL MEDICINE)

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CHENNAI- 600032

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TIRUNELVELI MEDICAL COLLEGE

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This is to certify that the dissertation entitled "**A COMPREHENSIVE STUDY OF PATIENTS ADMITTED WITH SNAKEBITE IN TIRUNELVELI MEDICAL COLLEGE HOSPITAL**" submitted by Dr. PARTHIBAN.D to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment for the award of M.D. Degree (GENERAL MEDICINE) is a bonafide work carried out by him under my guidance and supervision during the course of study 2016-2019. This dissertation partially or fully has not been submitted for any other degree or diploma of this university or other.

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DECLARATION

I solemnly declare that the dissertation titled "**A COMPREHENSIVE STUDY OF PATIENTS ADMITTED WITH SNAKEBITE IN TIRUNELVELI MEDICAL COLLEGE HOSPITAL**" is prepared by me**.** The dissertation is submitted to THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY towards the partial fulfillment of requirements for the award of M.D. Degree (Branch I) in General Medicine . I also solemnly declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree, diploma to any university, found either in India or abroad.

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PROTOCOL TITLE: A COMPREHENSIVE STUDY OF PATIENTS ADMITTED WITH SNAKEBITE IN TIRUNELVELI MEDICAL COLLEGE HOSPITAL
PRINCIPAL INVESTIGATOR: DR.D.PARTHIBAN, MBBS.,
DESIGNATION OF PRINCIPAL INVESTIGATOR: POST GRADUATE STUDENT
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Dear Dr.D.PARTHIBAN, MBBS., The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during The IEC meeting Held on 10.03.2017.

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☐
2.	Study Protocol	☐
3.	Department Research Committee Approval	☐
4.	Patient Information Document and Consent Form in English and Vernacular Language	☐
5.	Investigator's Brochure	☐
6.	Proposed Methods for Patient Accrual Proposed	☐
7.	Curriculum Vitae of The Principal Investigator	☐
8.	Insurance /Compensation Policy	☐
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☐
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☐
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of The validity
4. An annual status report should be submitted.
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6. At The time of PI's retirement/leaving the institute, The study responsibility should be transferred to a person cleared by HOD
7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in The original project. (Page no. Clause no. etc.)
   b. The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and The revised budget form should be submitted.
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STANDS APPROVED UNDER SEAL

Dr.K.ShantaramanMD
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CERTIFICATE – II

This is to certify that this dissertation work title **"A COMPREHENSIVE STUDY OF PATIENTS ADMITTED WITH SNAKEBITE IN TIRUNELVELI MEDICAL COLLEGE HOSPITAL"** of the candidate **Dr.PARTHIBAN.D,** with registration Number **201611358** for the award of **M.D.**Degreein the branch of **GENERAL MEDICINE (I).** I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion page and result shows 5**percentage** of plagiarism in the dissertation.

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CONTENTS

INTRODUCTION:

Being bitten by snake is frightening for all. Most of the snake bites produce little more than local pain and don't require medical attention. However some bites may produce life threatening complications hence seeking medical attention immediately after bite is mandatory to avoid mortality and morbidity.

The term venomous and poisonous are not the same. "Venomous" indicates organisms producing toxic material in the specialized gland and injecting through bite specialized venom apparatus and other means."Poisonous" refers to detrimental effects produced by touching or consuming plants/organisms. Poison found throughout the organisms but venom produced in isolated glands.

Most of the world's medically significant snakes belong to 4 familes – Vipiridae, Elapidaec, Colubridae and Atractaspidinae.In developing countries most of the snake bites occurs to the agricultural workers during their work in the fields. In developed countries most common victims are adolescent and young adults due to their risky behavior. >95% snake bites occurs over extremities.

Snake venoms are complex mixtures of proteins including enzymes and LMW polypeptides. The fear of snake bite itself produce symptoms like

nausea,vomiting,diarrhea,cold clammy skin,syncope regardless whether injection of venom.

In general VIPER bites cause deleterious effects on almost any organ system. Russell's viper is implicated in causing Acute kidney injury and neurotoxicity apart from the ususal local signs and coagulation abnormalities.In contrast ELAPIDAE family cause more neurotoxic manifestations with little or no envenomation.Exceptions are African pitting cobras (member of Elapidae family) produce little or no neurotoxicity but cause severe tissue necrosis and vipers like southern pacific rattlesnake (Crotalus oreganus helleri), Timber rattlesnake (Crotalus horridus horridus), Western diamondblack rattlesnake (Crotalus atrox), and Mohave rattlesnake (Crotalus scutulatus) produce significant neurotoxicity. Krait bites are commonly painless and produce neurotoxicity which won't resolve following administration of ASv or anticholinestrase because of post synaptic blockade. Sea snakes produce generalized rhabdomyolysis later leads to respiratory failure.

AIM OF THE STUDY

- To study the incidence of snake bite in patients admitted in TVMCH medicine department

- To study the incidence of toxic bite among all the snake bite patients admitted

- To study the commonest type of snake responsible for most of the snake bite cases.

- To study the practice of unauthorized method of treatments in snake bite patients.

- To study the various toxic manifestations of the snake bite (hemotoxic, neurotoxic and local reaction eg.cellulitis etc.)

- To study the complications arising during the patients stay in the hospital (AKI, compartment syndrome, DIC, respiratory failure etc.)

- To assess the features of autonomic arousal secondary to snake bite in acute bites like stress hyperglycemia, acute hypertension and electrocardiographic changes.

- To study the outcome and mortality rate in snake bites.

The study was conducted between may 2017 to april 2018.

REVIEW OF LITERATURE

Some venomous snakes are having bright attractive colours. This confers specific protection to the snakes of that species from natural predators. Some of the harmless nonvenomous snake may mimic the colours and behavior of venomous snake to get protection from preying predators, called (Batesian or Mullerian mimicry).

Venomous snake:

There are 3346 species of snakes in the world. Venomous snakes are broadly classified in to three families which include 667 species. These families are ***Lamprophiidae*** *(burrowing asps);* ***Viperidae*** (pit vipers and old world vipers); ***Elapidae*** (cobras, mambas, kraits, coral snakes, sea snakes).

The largest family of snake is *Colubridae*, includes 1748 species. Most of the species in this family is nonvenomous, only 100 species are capable of producing envenomation in humans (mild), rarely produce case fatalities.

Apart from producing case fatalities by envenomation, some of the snakes can kill humans by other mechanism. The giant constrictors (Family **Boidae)** usually kill their prey by wind around them. Similar manner these snakes will tightly circle around the torso of human, especially the children and adolescent,

producing constricting force severe enough to break the bones. Most of the victims die because of suffocation. There are fatal attacks by this family of snakes reported reliably in South-east Asian regions and south Americas. Some of the victims were swallowed.

Snake taxonomy:

Classification of snakes depends on variety of phenotypical characteristics. These morphological characteristics used for classification includes (numbers and arrangement of scales – lepidosis, osteology,sensory organs, mycology,dentition). Recently sequence analysis of DNA also used for classification.

Snake like animals:

Many animals might looks like snakes when first seen. When carefully examined show some differentiating features. Legless lizards and legless skinks can be distinguished by their external ears, eyelids, fleshy tongue and long tail. Some lizards might have vestigial limbs. Eels and pipe- shaped fish are distinguished from snakes by presence of gills and fins.

Medically important snakes:

Medically important snakes can be identified by possession of enlarged grooved or cannulated teeth (fangs) in the upper jaw. Venoms are injected into the prey and human victims through these fangs. Fangs may be placed posteriorly (opisthoglyphous) ex.some species of ***Colubridae*** , enlarged solid aglyphous (without central groove), the fangs may protruding from the corner of the mouth (solenoglyphous – hinged erectile fangs) ex.Stiletto snakes/ burrowing mole vipers/adders or the fangs may fixed erect (Proteroglyphous) ex.Elapidae family.

Elapidae *Family includes:*

cobras – *Naja*;

kraits – *Bungarus*

mambas – *Dendroaspis*

shield-nosed snakes – *Aspidelaps*

Viperidae family includes:

Crotalinae subfamily – pit vipers

Viperinae subfamily – old world vipers (futher classified into vipers which produce young snakes and adders which laying eggs).

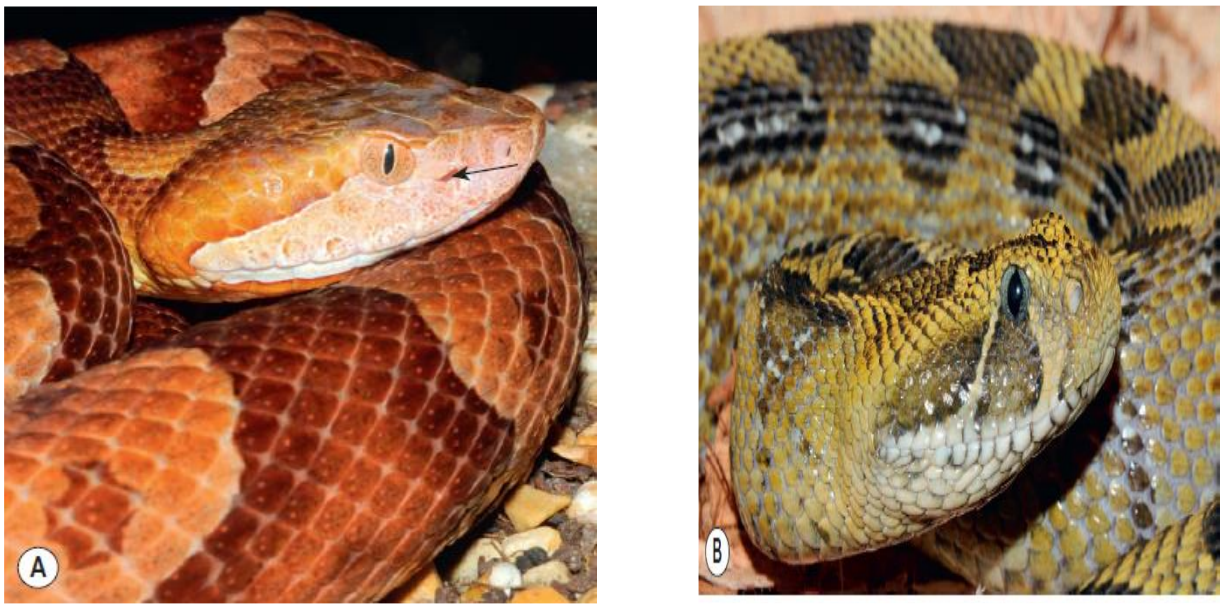

Fig 1 : A) Pit viper(North American copper head) showing heat sensing pit between the eyes and nostril
B) A old world viper (Ethiopian mountain viper) without the pit

Snake Identification:

There is no reliable and easy method to correctly distinguish venomous from non venomus snakes. Some of the snakes are correctly identified by the colour and pattern on their body and some by the characteristic behavior . For example cobras and some other elapidae family snakes produce characteristic hood when they take defensive attitude. Russell's vipers (Daboia russelii and D.siamensis) and puff adders (Bitis arietans) produce a loud hissing sound by exhaling air via their

nostrils; the saw scaled vipers ,lowland and desert horned vipers produce a rasping sound by rubbing their coils; Rattlesnakes produce unmistakable peculiar rattling sound by shaking their tails which was commonly mention as “Death Rattles”. There is a famous saying in the North America regarding identification of venomous and non venomous coral snakes, “ red on yellow kills a fellow, red on black venom lack”.

Fig 2 : characteristic hood produce by the cobra (species naja naja, belongs to Elapidae family)

Common species of snake found in different parts of the world resposible for most of human bites		
Area	Scientific name	Common name
North America	*Crotalus adamanteus* *Crotalus helleri* *Crotalus oreganus and Crotalus adamanteus*	Eastern diamondback rattlesnake Western rattlesnakes Western diamondback rattlesnake
South America	*Bothrops atrox,B.asper* *Crotalus durissus subsp.* *Bothrops jararaca*	Fer-de-lance,barba amarilla South American rattlesakes,cascabel Jararaca
Central America	*Crotalus simus subsp.* *Bohtrops asper*	Central American Rattlesnakes Terciopelo
Africa	*Echis Ocellatus, E.leucogaster,* *E.pyramidum, E.jogeri* *Naga nigricollis, Nl mossambica etc.* *Naja haje,* *Bitis arietans*	Saw scaled or carpet vipers Egyptian Cobra African spitting cobra puff adders
Europe	*Vipera berus, V. aspis* *Vipera ammodytes*	Vipers, adders Long-nosed or nose-homed viper
Asia, Middle East	*Echis spp.* *Daboia Palaestinae* *Naja oxiana* *Macrovipera labetina*	Saw scaled or carpet vipers Palestine viper Oxus cobra Levatnine viper
Indian subcontinent and South-East Asia	*Naja naja, N. kaouthia, N.stamensis, etc.* *Bungarus spp* *Daboia Russelli, D.siamensis* *Calloselasma rhodostoma* *Echis carinatus*	Asian cobras Kraits Russell's vipers Malayan Pit viper Saw scaled or carpet vipers
Far East	*Naja atra etc.* *Bungarus muticinctus* *Protobothrops flavoviridis* *Protobotriopsmucrosquamatus*	Asian cobras Chinese krait Japanese habu Chines habu

Australiasia, New Guinea	*Pseudonaja spp.* *Oxyuranus scutellatus* *Acanthophis spp.* *Notechis spp.*	Brown snakes Taipan Death adders Tiger snakes

Distribution of venomous snakes:

From sea level to altitudes of 4000 m (Gloydius himalayanus) venomous snakes are widely distributed. Venomous snakes are not found in some areas of the world. These include Antarctic, Arctic, Islands of Crete, Iceland and Ireland, New Zealand, Hawaii and elsewhere in pacific. Sea snakes commonly found in Indian and Pacific oceans from Latitudes 30^0N to 30^0S.

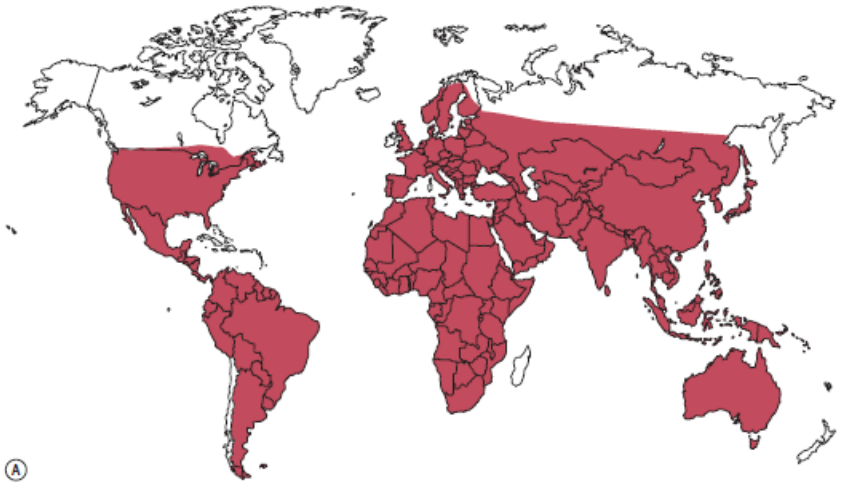

Fig 3: Distribution of venomous snakes around the world (A) Terrestrial snakes (B) sea snakes

Epidemiology of snakes:

Most of the bites are located in the lower limbs. Children and agricultural workers of tropical developing countries are predominantly affected. Increased incidences of bites are associated with rainfall.

ASIA:

In INDIA every year around 46000 people die from snake bites. Snake bites accounts for the 0.5 % of all deaths. 3% occurs in the age of <14 years; most of the victims was from the rural areas. Maximum deaths occur in the rural areas 97%, only 23% in a health facility. When the bite occurs during night during sleep

(between midnight -6 am) carries increased mortality, suggesting bites by kraits. Other risk factors for increased mortality were initial visit to a traditional healer and delay in seeking medical care.

Snake bite as occupational Disease:

In many tropical countries people with agriculture related occupations like Farmers, Plantation workers, Herders and hunters are at high risk of snakebites. In west Africa farmers are exposed to bite Echis species as they dig fields during rainy season. In South east Asia people are bitten by Malayan pit vipers (*Calloselasma rhodostoma*) when they go for early morning rounds of thr rubber trees in dark. During the periods of usage of hand nets for fishing fisherman are exposed to sea snakes bites in South east Asia which now became uncommon.

Bite Inflicted on Sleepers:

Kraits, In India, Thailand, Nepal, Sri Lanka, Malaysia and African spitting cobras enter human dwelling during at night while pursuing their prey and may bite those people who made movements during their sleep.

Venom Apparatus in Different Snakes:

Colubridae:

Only few species of this family is producing venom. In black fanged colubridae, the superior labial gland drains into buccal mucosa and tracks down through grooves in the anterior surface of posteriorly situated fangs. Human envenomation is uncommon because the snake needs to chew the finger of its victim in order to inject enough venom to produce symptoms.

Fig 4: Fangs of Back fanged Colubridae

Atractaspidinae:

The long fangs protrude from the corner of the mouth to allow side swiping hit at their prey. This arrangement is useful while encountering their prey underground

Fig 5 : Long fangs of Atractaspis aterrima (West African burrowing snake)

Elapidae:

Venom glands are surrounded by muscles in Viperidae and Elapidae. This arrangements help them to squeeze the venom through the duct to fangs.

“Dry bites”:

Non venomous bites from venomous snakes are called ‘dry bites’. Dry bites occur due to variety of reasons, including failure of venom delivery mechanisms and depletion of venom. 50% of all venomous snake bites, 20% of pit viper are dry.

VENOM COMPOSITION:

There are more than 100 different components in snake venom. The components vary among different species, even with same species in relation to different seasons and aging. This variation leads to florid manifestations and unpredictability following snake bites. More than 90% of the dry weight made up of proteins this includes, enzymes, non enzymatic polypeptide toxins and non toxic proteins. Other constituent of venom include carbohydrates, lipids , free amino acids, nucleosides and biogenic amines (serotonin) and metals.

Enzymes in snake bite includes, hydrolases, hyaluronidase and others like Phosphomono- and di-estrases, 5'nucleotidase, DNA-ase, NAD-nucleosidase,L-amino acid oxidase,phospholipase A_2 and peptidase. These are common for both Viperidae (89-95%) and Elapidae (25-70%) but the concentration differs. In addition to this Elapid venoms contain acetylcholine esterase, Phospholipase B and glycophosphatase and Viperid venoms have arginine esterase hydrolase kininogenase, endopeptidases, thrombin like serine proteases and factor X and prothrombin activating enzymes.

Phospholipase A_2 are the most common enzymes in venom. They produce damage to various biological structures includes, RBC, platelets, Leukocytes, Peripheral nerve endings, mitochondria, vascular endothelium and other membranes, skeletal muscles, produce opiate like sedative effects, presynaptic

neurotoxic activity and autopharmacological release of histamine. Spreading of venoms through tissues is promoted by hyaluronidase. Proteolytic enzymes like endopeptidases and hydrolases, produces local changes in vascular permeability causes edema, blistering and bruising and leads to necrosis. Metalloproteinases present in the produces their haemotoxic and myolytic manifestations by interfering with the functions of platelets, vascular endothelium, muscles and other tissues.

Neurotoxins:

Low molecular weight non – enzymatic polypeptide toxins are found almost exclusively in Elapid venoms. Post-synaptic (curaremimetic) neurotoxins also called α-neurotoxins , such as cobratoxin and α-bungarotoxin binds to post synaptic Nm acetylcholine receptors at motor end plates causing flaccid paralysis. These may leads to death from bulbar and respiratory muscle weakness. Presynaptic toxins (β-neurotoxins) eg.β-bungarotoxins,taipoxin and crotoxin contains phospholipase A_2 subunit. These toxins produce damage to nerve ending producing sequential suppression, enhancement and finally complete failure of release of acetylcholine by targeting voltage gated potassium channels. Both produce clilnicaly undistinguishable signs and symptoms and differentiated only

by their response to antivenoms and anticholinestarses. α- neurotoxins responds well to the treatment but not the β-neurotoxins.

Mamba venoms contain some unusual neurotoxins. These includes,

1. Dendrotoxins – acts on voltage gated potassium channels causing release of acetylcholine.
2. Calcicludine – Blocks calcium channels
3. Fasciculins – Inhibits acetylcholineestrases
4. Calciseptine – binds to calcium channels.

Krait venoms are important for neuropharmacologists. They are used for various research puposes. They contain,

1. Presynaptic phospholipase A_2 (β-bungarotoxins)
2. Postsynaptic α-neruotoxins
3. κ-bungarotoxins – binds to nicotinic ach receptors in the brain and ganglia.

Cardiovascular Toxins:

Snake venoms produce variable cardiovascular manifestations. Including,

1. **Hypotension** – by variety of mechanisms such as increased permeability and hypovolemia, increased production of bradykinin, decreasing conversion of angiotensin I to angiotensin II (basis for synthesis of ACEI). Some species (Istaelin burrowing asp) produe Sarafotoxins which has 60% homology with endothelins leads to the coronary vasoconstriction and AV blocks. Some peptides in the snake venom has got natriuretic property.

Clinical features of Envenoming:

Local envenomation:

1. Swelling and bruising – due to increase vascular permeability Produced by venom phospholipases, metalloptoeinases, membrane damage polypeptide chains.
2. Tissue necrosis – caused by cytotoxins and myotoxins. Secondary effects of tourniquets and first aid methods also contribute to tissue necrosis.

Hypotension and Shock:

1. Produced by Extravasation of plasma and blood
2. Massive GIT haemorrhage or uterine haemorrhage
3. Splanchnic vasodilatation
4. Direct effect of toxin over mycocardium
5. Autopharmacological syndrome caused by release of vasoactive compounds such as nitric oxide, Kinins, histamine, serotonin and endothelins.

Coagulation Disturbances:

- Commonly seen after Viper bites
- Consumptive /Venom coagulopathy results from activation of intravascular coagulation by procoagulant enzymes along with activation of endogenous fibrinolysis by plasmin. Prothrombin activators, Factor X activators and thrombin like enzymes are the commonly found procoagulants.
- Haemorrhagins causes vascular endothelial damge producing spontaneous bleeding.

- Platelet activation/ inhibition : Toxins in the snake bite venoma activate/inhibit the GPVI,GPIb,GPIbα,GPIa-IIa and other platelet receptors.
- Complete activation by aternate pathway (Colubridae and Elapidae venoms – cobra venom factor C3b) or classical pathway (vipered venoms)

Acute Kidney Injury (AKI):

It commonly occurs after bitten by Russell's viper, sea snakes and Rattle snakes. Mechanism of Acute Tubular Necrosis includes,

1. Hypotension and hypovolemia
2. DIC
3. Microangiopathic haemolysis
4. Haemoglobinuria, Myoglobinuria
5. Direct toxic effect of toxin on tubular cells

   Various histopathological renal changes noted following snake bite includes, proliferative glomerulonephritis, fibrin deposition, toxic mesangiolyisis with platelet agglutination, distal tubular damage ('lower nephron nephrosis'), ATN, renal cortical necrosis.

Neurotoxicity:

It is the characteristic feature of envenomation by most elapids, such as Cobras, mambas, coral snakes, kraits but not the African spitting cobras which produce predominant local effects without identifiable neurotoxicity. Russell viper also produce neurotoxic manifestations in humans.

fig 6: ptosis due to nerutoxic envenomation following cobra bite (Naja naja)

The most common mode of death following neuotoxic snake bite is respiratory paralysis. But death can also arise from upper airway obstruction and aspiration due to bulbar paralysis. Anticholinesterases may reverse the effects of snake bites with predominantly post synaptic toxins (α – neurotoxins) for example Indian Cobras,coral snakes. Some Elapids or vipers venom specific components which releases endogenous opiates producing drowsiness in patient without respiratory failure.

Rhabdomyolysis:

Phospholipase A2 is responsible for the generalized rhabdomyolysis and release of myoglobin, muscle enzymes, uric acid and pottsium into the blood stream. Krait usually produce no local damage except for the three species, Bungarus niger,B.fasciatus, B.caniddus.

Venom opthalmia:

Some of the snakes can spit venom into the eyes of their prey and victims,such as Spitting cobras and rinkhals. This venom produce damage to the mucous membranes when come into contact. Produce various manifestations like anterior uveitis, corneal erosions and secondary infections.

Envenoming by Different families of snakes:

COLUBRIDAE (BACK-FANGED SNAKES):

Most of the species in this family produce mild local signs. Only few are capable of producing life threatening envenomation. These includes,

Fig 7: Twig tree or bird snake (Thelotomis mossambicanus family colubridae)

- Boomslang (Dispholidus typhus) - In Africa
- Vine,twig,tree or bird snake (Thelotornis spp..) - In Africa
- Yamak agashi (Rhabdophis tigrinus) - In Japan
- Red necked keelback (R.subminiatus) - In Southeast Asia

Symptoms may be delayed upto days after the bite. The major symptoms include nausea,vomiting, headache and colicky abdominal pain. Bleeding manifestations includes, bleeding from the bite site, old and recent wounds, epistaxis, gingival bleed, melaena, haemetamessis, SAH, ICH and extensive echymoses. DIC and AKI can also occur. Majority of deaths attributed to AKI which develop days later the bite.

ATRACTASPIDINAE: (STILETTO SNAKES, NATAL BLACK SNAKES, BURROWING ASPS):

There are 17 species identified so far. All are venomous but only 3 species fatal envenomation, A.irregularis, A.engaddensis and S.microlepidota. Atractaspis venom was described to have very high toxicity when compared to other family of snakes. Local signs of envenomation include pain, swelling, necrosis, local numbness or parasthesia, local lymphadenopathy. Death occurs in the victims within 45 minutes bite due to vomiting, profuse salivation and coma due to violent autonomic activation. ECG abnormality includes Prolonged PR interval and ST-T changes. Mild alteration in liver function and blood coagulation also noted.

ELAPIDAE:

This family contains,

1. *Cobras*
2. *Kraits*
3. *Mambas*
4. *Sea kraits*
5. *True sea snakes*
6. *Mambas*
7. *Coral snakes*

Fig 8: Greater black krait (Bungarus niger)

- **Local envenomtion ,** following most of the species are mild and neglible but exception do occur. African spitting cobra produce extensive local necrosis and bite by King cobra (Ophiophagus Hannah) produce swelling of whole limb with bullae at bite site without prouduce significant necrosis.

Fig 9: Texas coral snake (Micrurus tener)

- **Neurotoxic effects**, Descendin flaccid paralysis is common following cobra bite. The earliest symptom of envenomation is vomiting which is usually repeated. Other early symptoms include blurring of vision, paraesthesia around the mouth,

headache, dizziness, hyperacusis, contraction of frontalis and signs of autonomic nervous system activation (goose flesh, conjunctival congestion, hypersalivation).

Paralysis intialy begin as ptosis and external ophthalomplegia. Theses can be evident within 15 minutes of bite in case of cobras and mambas or delayed upto 10 hours are more in krait bites. Later paralysis of facial,pharyngeal,jaw muscles are develops. Intercostals muscles affected before the limb mucles and diaphragm. Loss of consciousness and seizures can be explained by hypoxia produced by respiratory muscle paralysis. Intractable hypotension can also occur.

Fig 10: Indian cobra (Naja naja)

Neurotoxic effects are completely reversible after antivenom or administration anticholinestrase or they wear of spontaneously. Recovery time of varies muscles vary,

Diaphragm - 1-4 days

Ocular muscles - 2-4 days

Full motor recovery - 3-7 days

SEA SNAKES:

The bites are usually painless. The predominant feature is the generalized rhabdomyolysis. Initially victims develop headache, sweating, thirst, thick feeling of the tongue and vomiting. Generalized body ache and muscle pain develops between 30 mins to 3.5 hours. Trismus is common feature. Later progressive flaccid paralysis of muscles occurs as in elapid bite, the patient remain conscious until the respiratory failure occurs.

Myoglobinaemia and myoglobinuria develop 3-8 hours after the bite. The plasma turns brown when this occurs. Urine became cola – coloured. Hyperkalemia develops within 6-12 hours of bite due to potassium released from damaged muscles. Myoglobinuria and hyperkalemia produce renal failure. Hyperkalemia can also precipitate cardiac arrest.

VIPERIDAE :

This family includes,

1. Old World vipers and adders
2. New World Pit vipers
3. Asian pit vipers
4. Lance-Headed vipers
5. Rattlesnakes
6. Moccasins

Local envenoming. Vipers produce severe local effects within minutes of bite rarely delay occurs in onset symptoms. There will be rapid spread to involve entire limb even the trunk. Persisting bleeding from the fang marks is so common. Pooling of blood in the swollen limb can leads to hypovolemic shock.

Fig 11.1: Russell's viper (Daboia russelli)

FIG11.2: cellulitis following Russell's viper bite

The local effects following the viper bites are so common that the absence of detectable swelling within 2 hours of bite can be taken as no venom been injected[M]. As there is no exceptions for exceptions, bite by Burmese Russell's viper (Daboia siamensis), tropical rattlesnake (Crotalus durissus terrificus) and Mohave rattlesnake (Croatalus scutulatus) produce systemic envenomation without significant local signs.

Haemostatic Abnoramlities. These are characteristic feature of viperidae. Prolonged bleeding >10 minutes from the bite site, from the old and new injuries and from the venupucture site indicates consumption coagulopathy. Spontaneous systemic bleeding first detectable at the gingival sulci. Other types of spontaneous bleeding includes,

- Haematuria
- Bleeding into the floor of the mouth
- Bleeding into the tympanic membrane
- Ecchymosis
- Intracranial bleeding
- Subconjunctival haemorrhage
- Bleeding gums, epistaxis

- GI bleeding
- Genitourinary tract bleeding

Fig 12 : Saw scaled viper (Echis Carinatus)

Sometimes envenoming may produce major areteiral thrombosis. This was documented following the bites of Bothrops lanceolatus, B.caribbaeus,Daboia siamensis,D.russelii, Crotalus helleri[3].

Acute kidney Injury.

Common after bitten by Russell's viper,tropical rattlesnake and some species of Bothrops. After bitten by Russell's snake patients become oliguric within few hours, loin pain develops within a day, became irritable and develop hypertensionin 3-4 days and become comatosed secondary to metabolic acidosis.

Neurotoxicity. Usually produced venom phospholipase A_2. It is commonly seen after bite of tropical rattle snake, Russell's vipers, Gloydiums blomhoffi,G.brevicaudus,Bitis atropos. Paralysis was descending type as in Elapid envenomation.

Interval between bite and Death:

Elapids – within hours of bite

Sea snakes - 12-24 hours

Vipers - within days

Laboratory investigations:

- **The 20 minute whole Blood Clotting Time (20WBCT):**

Prolonged WBCT is the major sign of envenomation of Viperidae and Australian Elapidaes and medically important Colubridae family snakes.

IT is a simple bed side all or none test. Here the few milliliters are collected in clean,dry,glass tube and kept in a room temperature for 20 minutes without any disturbance. At the end of 20 mins the tube was tilted to appreciate clotting. It is must to use the glass tube inorder to activate Hageman factor (FXII). Other test

which can be performed depends upon availability of test. These includes, INR,D-deimer, Fibrin Degradation Products (FDP)

Serum levels of aspartage transaminase, ceraitine kinase,blood uea, myoglobin, potassium, ABG are other relevant investigations should be done for the patients presenting with cellulitis or Acute renal failure.

- **Imaging:**

Ecg may reveal sinus tachycardia, sinus bradycardia, various Blocks, evidence of hyperkalemia and myocardial ischemia or infarction.

Chest X Ray may reveal pulmonary edema, pulmonary hemorrhages and infarcts, pleural effusion and secondary bronchopneumonia.

CT and MRI imaging are useful in identifying Intra cranial haemorrhages and infarcts in patient with focal neurological signs.

USG reveals pericardial effusion, myocardial dysfunction and retroperitoneal bleeds.

- **Immunodiagnosis:**

Detection and Quantification of venom antigens is a valuable research tool for identification of species responsible for envenomation and severity of envenomation and asses the prognosis and effectiveness of antivenom. But this

modality is not easily available and has financial restriction. It has got very high sensitivity but specificity is inadequate in differentiating different species in same genus or closely related genera.

PCR detection of venom gland mitochondrial DNA from the wound site is the highly specific method for identifying bitten species.

Management of Snake bite:

First Aid:

This must be carried out by the victims themselves or by the people nearby to them, immediately by available resources. It comprises of

1. Reassuring the victim
2. Immobilize the affected limb to prevent the if possible whole patient to prevent systemic absorption. Application of pressure immobilization may be useful for the same. But application of tight rings, bracelets and tourniquets are strictly contraindicated.
3. Place the patient in recovery position if vomiting present to prevent aspiration.
4. Wash the bite site with running tap water and soap
5. Transport the patient to nearby healthcare as early as possible by means of motor vehicle, boat or stretcher.

6. Avoid harmful and time wasting treatments
7. If the snake was captured or killed it should be taken along with the patient for identification. It must be kept in mind even the death snake might be able inject venom after hours of dead in some species! (e.g. Rinkhals – Hemacatus haemachatus)

Pressure immobilization (PI) :

This is Effective in delaying absorption of venom into circulation. Experiments regarding benefits of Pressure bandage had conducted by Struan Sutherland in Australia among restrained monkeys. It showed successful results, even though no formal clinical trials were available, by means of delayed systemic envenomation and rapid deterioration of patients following the removal of the bandage. The aim is to exert of 55 mmHg of pressure which is sufficient enough to block lymphatics and venous drainage through which larger molecular weight toxins spread without compromising arterial supply to the affected area. But the concern regarding increase in intracompartmental pressure which might potentiate to necrotic effects of some snake venom discouraged its use. But there is no valid proof exist for this issue clinically or experimentally.

Victims of Elapid bite usually develop respiratory paralysis on arrival at the hospital. PI is therefore should be applied immediately in all cases of suspected Elapid bite in order to delay the systemic toxicity and death during transit.

Application of glyceryl Trinitrate ointment to the bitten limb slowed the lymphatic flow. So it can be used for delaying systemic envenomation.

Don’t Do’s in case of Snake bite:

- Cauterization, incision, suction by mouth, amputation of bitten digit, vacuum pumps are absolutely contraindicated because they produce harmful effects and delay in seeking medical attention.
- Application of Ice packs, snake stones, electric shock , or chemical compounds such as potassium permanganate are contraindicated because of no proven benefits even worsen the condition
- Application of tight tourniquets increases the morbidity and mortality among snake bite victims hence never recommended
- Incision produces uncontrolled bleeding in the presence of coagulopathy and introduces secondary infections.
- Ice packs, chemicals and suction at bite site produce tissue necrosis.

Treatment of Early symptoms:

Local pain:

Paracetamol, codeine or stronger opiods are advised. NSAIDs are better avoided because of the risk of gastric bleeding in the setting of coagulopathy.

For **vomiting** patient should be placed in the recovery position for preventing aspiration. For recurrent vomiting IV or rectal Chlorpromazine (25-50 mg in adults, 1mg/kg in children) is recommended.

Anaphylaxis should be treated with adrenaline 0.1% (0.5 ml IM in adults - 0.01 mL/Kg in children). The role of antihistamincs administered at a dose of (10 mg in adults, 0.2mg/kg in children) by IV or IM route and Hydrocortisone is not proven.

Respiratory Distress:

This may because of upper airway obstruction or from respiratory paralysis. Patients should be placed in a recovery position, airways should be cleared. If supplementary oxygen provides no benefit immediately artificial ventilation initiated via Endotracheal Tube, tracheostomy or supraglottic airway. Non Invasive Ventilation (NIV) by ambu bag and anaesthetic mask is rarely useful. If patient developed cardiac arrest CPR should be initiated.

Assessment on arrival to the Medical Facility:

Snake bite is a medical emergency. Following four questions are answered first on arrival to determine the condition of the bite and nature of envenomation,

1. Site of snake bite (to look for signs of local envenomation)
2. Time of snake bite (to carefully monitor for the development of signs)
3. Where was the bite take place and how did the snake look like (give rough idea about the type of snake e.g. bite occurring at night during sleep and indoors are commonly due to kraits)
4. How the patient feeling at present (to assess the symptoms of envenomation)

Apart from this ask for any native treatment undertaken before reaching to the medical care. Is there any history suggestive bleeding, syncope, visual disturbances and urine output since bite all give the valuable information regarding need for intensive care.

Before removal of any applied tourniquets or pressure bandage patient must be put up with IV line for resuscitation if any deterioration occurs. The visible fang marks strongly indicates bite but its absence never exclude the possibility of snake bite. Local warmth, swelling, tenderness and regional lymphadenopathy are the earliest sign of envenomation.

Since gingival sulci is the earliest site of spontaneous bleeding it must be examined initially. Look for Ptosis which indicates the neurotoxic envenomation. But it must be distinguished from fatigability induced ptosis by asking the patient to look upwards which resolve the later but true ptosis persist. Even before the appearance of ptosis subtle clinical signs can be elicited as to indicate envenomation. These include contraction of frontalis muscle (producing raised eyebrows and puckered forehead) and backward head tilt.

If the patient developed shock secondary to increased permeability of the vascular compartment or due to bleeding into extravascular compartment (retroperitoneal space, GI bleed, genitourinary bleed, bleeding into the swollen limbs) the foot end of the patient should be elevated and bolus of IV fluids administered. Early hypotension may be related to vasodilatation and should be treated with normal saline boluses of 20ml/kg repeat for 3 times. If not corrected with volume expansion initiate vasoactive pharmaceuticals agents such as epinephrine or dopamine (in addition to ASV as appropriate) Monitoring the response with jugular or central venous pressure is ideal. If shock is attributed to Anaphylactic reaction to venom initiate treatment for anaphylaxis (antihistamines, steroids, epinephrine) earlier

Patients with generalized rhabdomyolysis will have trismus, severe muscle tenderness which is resistant to passive stretching. Patient also develop decreased urine output or high coloured urine and neuromuscular weakness.

If the snake was identified and found to be non venomous patient can be discharged with tetanus shot. If the offending snake is unidentified patient should kept under observation for the period of 24 hrs even the initial assessment showed no signs of envenomation.

Antivenom

Also known by several names such as **Antivenin, Antivnene, Anti Snakebite Serum, Anti snake venom – ASV**

This is prepared from the serum of animals (e.g. horses and sheep) after immunizing them with one or more venoms. These are actually the Immunoglobulin formed in the animals against the injected venom. The most important decision to make in snake bite is whether to administer the ASV or not. Early administration of ASV prevents the morbidity and mortality drastically. But there is high risk of developing severe anaphylactic reactions following the ASV administration. Hence the decision should be made after concerning varies factors like signs of envenomation, duration since bite, type of snake, components of antivenom, previous history of anaphylaxis and availability of adequate measures

to counteract the anaphylactic measures when it occurs. But with pt who presented early with signs of envenomation ASV is the only proven antidote. But it always should kept in mind that only minority of snake bitten patients actually require Antivenom.

ASV should be administered early in case of significant envenomation because it is capable of neutralizing only circulating, unbound venom in the blood. There is no benefit in giving ASV at local bite site.

ASV is available in liquid form as well as in lyophilized form. Prepared ASV placed in a solution (Generally NS equivalent to 20ml/Kg body weight). Although more prone for allergic reactions (since it is an heterologus serum product) Skin test prior to administration is not indicated due to its unreliability

Indications for Antivenom:

1. Haemostatic abnormalities :
    a. Spontaneous bleeding
    b. Incoagulable blood (20 WBCT) or prolonged clotting time
    c. Elevated FDP or D-dimer
2. Cardiovascular abnormalities:
    a. Hypotension

b. Shock

c. Cardiac arrhythmia

d. Reduced Ejection Fraction (EF) in echocardiogram

3. Neurotoxicity:

    a. Ptosis

    b. Bulbar paralysis

    c. Complete paralysis

    d. External ophthalmoplegia

    e. Fasciculations

4. Black coloured urine due to rhabdomyolysis or DIC

5. Patient with definite local envenomation with following features which suggest systemic envenoming:

    a. Leucocytosis

    b. Elevated creatine kinase and aminotransferase

    c. Uraemia

    d. Haemoconcentration

    e. Oliguria

    f. Hypoxemia and acidosis

In the absence of above 5 indications rapid swelling involving more than half of the bitten limb or extensive blistering or bruising, enlarged tender regional

lymphadenopahy and patient bitten by snakes which known to produced extensive necrosis are the indicaction for administration of ASV.

Contraindications for ASV:

There are no absolute contraindications for severely envenomed patients. There are some relative contraindications are there includes,

1. Atopic patients
2. Those who had previous allergic reactions to ASV

If signs of sever life threatening envenomation were present pretreatment with adrenaline 0.01% solution 0.25ml SC followed by empirical antihistamine and steroids given IV is recommended. Patient must be kept in observation 3 hrs after the completion of infusion.

If the snake identified monovalent Antivenom is preferred over the Polyvalent ASV. Polyvalent ASV usually contains antiveom for the most important species present over the give geographic region.

Expiry dates:

Useful activity may be retained for years after the stated expiry date by the manufacturer. Liquid lyophilized antivenom retain most of their activity for more than 5 years if properly stored below 8^0C. Solutions that are opaque or having suspended particles are should not be given, as precipitated proteins indicate loss of activity.

Indian Anti Snake Venom:

The Indian antivenom manufacturers prepares "polyvalent anti-snake venom serum" using the venoms of the four most important venomous snakes in India (Indian cobra, Naja naja; Russell's viper, Daboia russelii; saw-scaled viper, Echis carinatus Indian krait, Bungarus caeruleus;), although the validity of the concept of "the big four" is subjected to questions by the discovery of the importance of other species to produce clinically significant envenomation in certain regions.

Fig 13: ASV produced by Indian Manufacturer's

In India ASV is supplied in liquid as well as in freeze dried form. The freeze dried powder is reconstituted with 10 ml of sterile water for injection which is supplied with the pack. The powder dissolved into a clear colourless or pale yellow liquid.

Each ml of reconstituted ASV is capable of neutralizing the venom of the following species of snake.

- Indian cobra (Naja Naja) – 0.60 mg dried venom
- Common krait (Bungarus Caeruleus) - 0.45 mg
- Russell's viper (Daboia russelli) - 0.60 mg
- Saw scaled viper (Echis carinatus) - 0.45 mg

Time of administration of ASV:

ASV should be given as early as possible to elicit the maximum benefit. But the there is no definite cut off limit for administration of ASV. It is never too late to administration of ASV as long as there is signs of envenomation (coagulation abnormality can persist for 2 days after sea snake bite and days to weeks after bite by viperidae family). But local effects of envenomation are not reversible if ASV is delayed more than few hours.

Route of administration of ASV:

Intravenous route is preferred. An infusion over 30-60 mins is ideal than the direct Iv administration of undiluted antivenom 1-2ml every 10-20 mins. But there is no difference in effectiveness or development of adverse reactions in these two method. But the former one is convenient and easy to administer in clinical point of view. Intramuscular route bioavailability is very slow and incomplete hence not preferred ideally. But in case of emergency, where no one is skill enough to secure the intravenous access Intramuscular route may be the next best choice. Preferred site for IM injection is anterolateral aspect of thigh not the gluteal region followed by massage of injected site to promote absorption and prevent hematoma formation. Local administration of ASV over the bite site is generally not

advocated as it may increase the intracompartmental pressure and aggravate tissue necrosis.

Initial Dose:

There is no fixed dosage available for initial administration. The dosage varies with the species and depends of the severity of envenomation. The apparent half life of antivenom in patients with envenomation ranges from 26 to 95 hours. The dosage of ASV for the adult and children remain the same because the amount of venom injected will be the same in both. Initial dose needed for some important species are give in following table.

Guide to Initial dosage of antivenom			
Snake species		**Antivenom**	
Latin name	**English name**	**Manufacturer**	**Approximate initial dose**
Acanthophis spp.	Death adders	CSL,death adder or polyvalent	6000 – 18000 units (1-3 vials)
Bungarus caeruleus	Common krait	Indian manufacturer,polyvalent	100 ml

Bungarus fasciatus	Banded krait	TRC banded krait antivenin or 'neuropolyvalent'	50 ml
Bitis arietans	African Puff adders	SAVP, polyvalent Sanofi Pasteur polyvalent	80 ml
Bothrops atrox	Common lancehead	Brazilian manufacturers, Bothrops Polyvalent	2-12 vials
Daboia Russelli	Western Russell's viper In	Indian manufacturer,polyvalent	100 ml
Daboia siamensis	Eastern Russell's viper (Thailand)	TRC Russell's viper antivenom 'hemato-polyvalent'	50 ml
Dendroaspis species	Mambas	SAVP Dendroaspis or polyvalent	50-100 ml
Echis carinatus Asia	Asian saw scaled viper	Indian manufacturer,polyvalent	50 ml
Naja Naja, Naja oxiana	Indian cobras	Indian manufacturer,polyvalent	100 ml

Observation of the response to antivenom:

If the dosage of ASV is adequate, the following responses may be observed.

(a) General: The patient feels better. Nausea, vomiting, giddiness, abdominal discomfort headache and generalized aches and pains may disappear very quickly. This cab be explained partly by placebo effect to the treatment administered.

(b) Spontaneous systemic bleeding (e.g. from the gums): Bleeding from the various sites usually stops within 15-30 minutes.

(c) Blood coagulability (as measured by 20WBCT): Normalisation of WBCT occurs in 3-9 hours. Bleeding from new and partly healed wounds usually stops earlies than the correction of WBCT.

(d) In shocked patients: Rise in blood pressure may observed within the first 30-60 minutes of ASV administration and arrhythmias such as sinus bradycardia may resolve.

(e) Neurotoxic envenoming of the post-synaptic type (cobra bites) may show improvement as early as 30 minutes after antivenom, but usually takes hours for significant improvement. Envenoming with presynaptic toxins (kraits and sea snakes) will not respond similar way and anticholinestrase will show benfits in the cobra bites not with the kraits and sea snakes.

(f) Active haemolysis and rhabdomyolysis may terminate within a few hours and the colour of urine changed from cola colour to normal.

Recurrent envenoming:

It is defined as occurrence of clinical and laboratory features of systemic envenomation several days after the initial good response to antivenom. The probable mechanisms includes, continuing absorption of venom from the injection site or redistribution of venom from tissues. Venom absorption may be increased after the recovery of patient from shock.

Repeated dosing:

The initial response to ASV determines whether further doses are needed or not. Neurological symptoms improve 30-60 mins of administration of ASV and clotting time normalized within 6 hrs. So persistent of cardiorespiratory symptoms for more than 60 mins and clotting abnormalities more than 6 hrs necessitate the second dose administration.

The ‘6-hour Rule’:

In case of consumptive coagulopathy the liver start synthesizing clotting factors in response to circulating fibrin degradation products and normalize the clotting abnormality usually within 6 hrs. This formed the basis of testing blood every 6 hrs who presented with coagulopathy till the abnormality normalize. After that, WBCT checked every 12 hours for next 48 hours.

Antivenom reactions:

They are classified into Early (anaphylactic), Pyrogenic or late (serum sickness) type.

Early reactions: This includes,

- Itching
- Urticaria
- Fever
- Tachycardia, palpitations,
- Cough
- Nausea and vomiting
- Brochoconstriction
- Angio edema
- Hypotension

Febrile reactions:

Due to contamination during manufacturing of antivenom. Patients develop high fever and rigors 1-2 hours after treatment, vasodilation and fall in blood Pressure.

Late reactions (Serum sickness):

ASV can cause delayed IgG/IgM mediated serum sickness 1-2weeks after administration manifesting as fever,myalgia, arthralgias,urticaria , renal and neurological involvement. It can be easily treated with oral antihistamines (chlorpheniramine 2mg qid in adutlt; In children 0.25mg/kg/day in divided doses), steroids (5 mg four times a day for 5 days in adults; 0.7 mg/kg/day in divided does for 5 days in children) and acetaminophen.

If reactions occur stop the infusion and initiate antianaphylactic measures and restart at a slower rate in a more dilute solution. If severe reactions persist assess the risk benefit ratio if ASV is still deemed critical place patient in intensive care unit and infuse ASV and Epinephrine simultaneously.

Supportive care:

Patient with neurotoxic envenomation may require ventilator support. Neostigmine can be given intramuscularly at a dose of 0.02mg/kg in adults and 0.04mg/kg in children. Before that patient should be atropinised to prevent unwanted muscuarinic features. If improvement occurs neostigmine methylsulphate can be administered every 0.5-2.5 mg every 1-3 hours upto 10mg/day in adults or 0.01-0.04 mg/kg every 2-4 hrs for children by IM /IV/SC route.

Local infection and Compartment Syndrome:

Prophylactic antibiotics are contraindicated unless the wound is incised or there is evidence of necrosis. Swelling of muscles within the tight compartment produces compartment syndrome. Classical signs include excessive pain, pain on passive movement, weakness of compartmental muscles, hypoesthesia of skin supplied by nerves running through the compartment and tense compartment.These are usually remembered by the 7Ps'

- Pain at rest
- Pain on passive movement

- Paralysis
- Pallor
- Parasthesia
- Poikilothermia
- Pulselessness.

Prevention of snake bites:

- Community education of safe walking by wearing foot wear and using light while walking through dark
- Sleeping on raised bed or if impracticable use well tucked in mosquito bed net.
- Avoiding the high risk habitatis in relation to time of day, seasons of the year
- Take cautious approach while collecting logs, moving boxes or swimming in a overgrown lakes and rivers.
- Domestic animals like chickens and rodents attract snakes. So maintain safe distance and make rodent proofing by removing unnecessary junks and litters.

- Chemicals like naphthalene, sulphur, insecticides and plants like ‘Indian Snake Root’ may be used to repel the snakes.

MATERIALS AND METHODS:

SAMPLE SIZE:

All the snake bite cases admitted in TVMCH during the study period of one year.

No of Patients studies : 403 patients

Study period : 1 year (From 1st may 2017 to 30th april 2018)

Study type : Descriptive Study

INCLUSION CRITERIA:

1. All known cases of snake bite patients admitted in TVMCH during the study period
2. All the referred cases of snake bite patients from nearby PHC/ hospital with complications
3. Age group > 12 years
4. All known case of bronchial asthma, COPD without any acute exacerbation prior to snake bite
5. All the cases of ischemic heart disease/ diabetes / hypertensive/ epilepsy with snake bite

EXCLUSION CRITERIA:

1. Age < 12 years
2. Doubtful bites (patient not sure about what bite them)
3. ? snake bites (patient found snake beside them at night)
4. Known cases of haemophilia and other coagulation disorders
5. Known cases of CKD / who already undergoing dialysis
6. Known cases of sepsis with AKI (before the incidence of snake bite)
7. Known cases of patient with cellulitis in the same limb due to other causes apart from snake bite.
8. Known cases of COPD patients with severe respiratory distress
9. Known cases of bronchial asthma with previous episodes of status asthmaticus presenting with respiratory failure onset before the snake bite

METHODOLOGY:

Informed consent was obtained from the patients for taking part in this study. Patients who are selected on the basis of inclusion and exclusion criteria were followed since the day of admission till the final end point (Discharge/ Death). The Type of snake, place of bite, history of any unauthorized treatment, time delay between bite and seeking medical attention, predominant presenting symptoms are obtained from history and with the help of photographs. All the patients were subjected to WBCT and neurological examination. Those who showed some abnormalities in laboratical value were subjected other special investigations according the need.

Outcome of the patient were assessed according the history, comorbid conditions and complications secondary to snake bite.

STATISTICAL ANALYSIS:

Statistical analysis was done using **simple percentage analysis, CHI SQUARE TEST**

OBSERVATION AND RESULTS

In our study 403 Snake bite patients were selected during the one year period (from May 2017 to May 2018) based on inclusion and exclusion criteria , observed and subjected to relevant investigations and results are compiled.

TABLE 1: SEX WISE DISTRIBUTION

Gender		N	Mean	Std. Deviation	Percentage
Age	Female	262	40.42	16.62	35%
	Male	141	44.01	16.02	65%

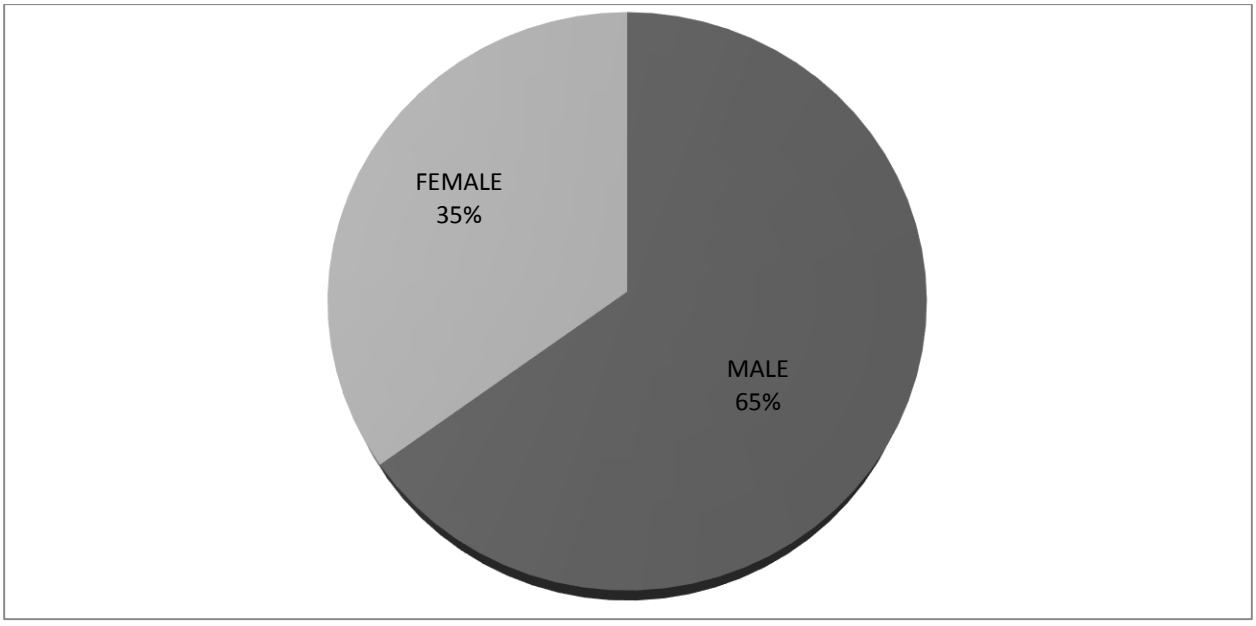

Figure 1 : Sex wise distribution of Snake bite

In our study males (65%) are found to have more incidence of snake bite than females(35%)

TABLE 2: PLACE OF SNAKE BITE

		No of patients	Percentage
Place of bite	Indoor	19	4.7%
	Outdoor	384	95.30%

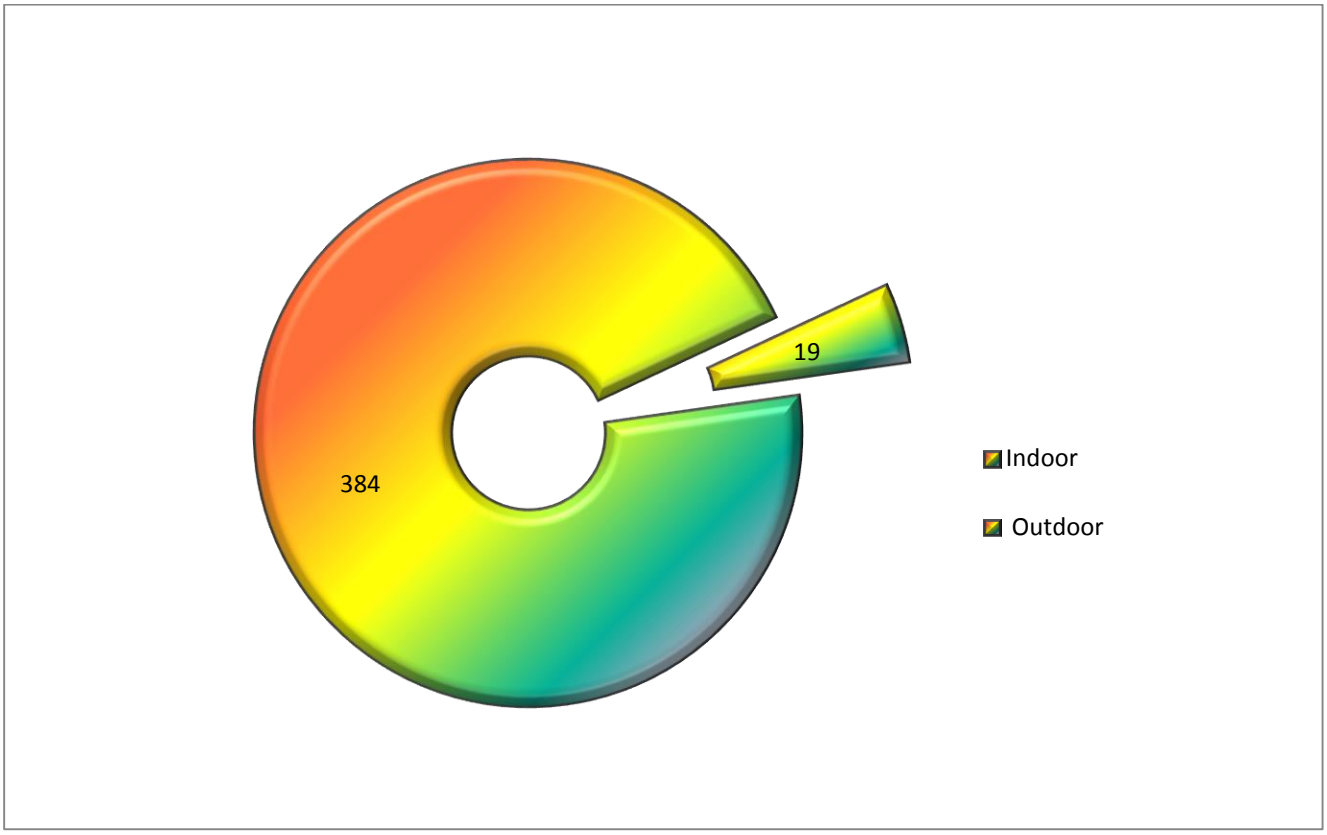

Figure 2: Place of snake bite

In our study most of the patients had the snake bite when they were outside of their home.

Table 2.1: Native treatment

Native treatment	No of patients	Percentage
YES	20	5%
NO	383	95%

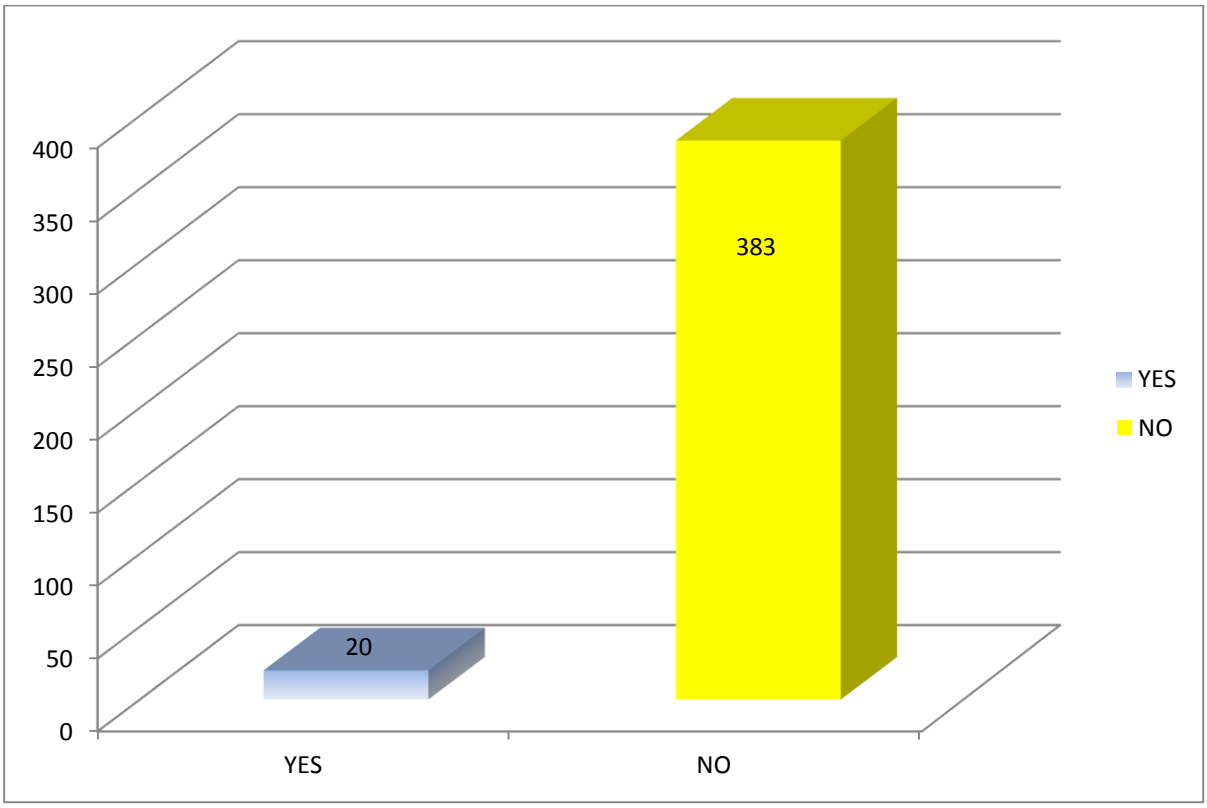

Figure 3: Native treatment

Among the 403 snake bite patients we studied around 5% of people (20) underwent some form of unauthorized method of treatment before seeking medical care.

Tab 2.2: Native treatment and outcomes

Native treatment	No of patients	Percentage
Morbidity	4	20%
Mortality	2	10%

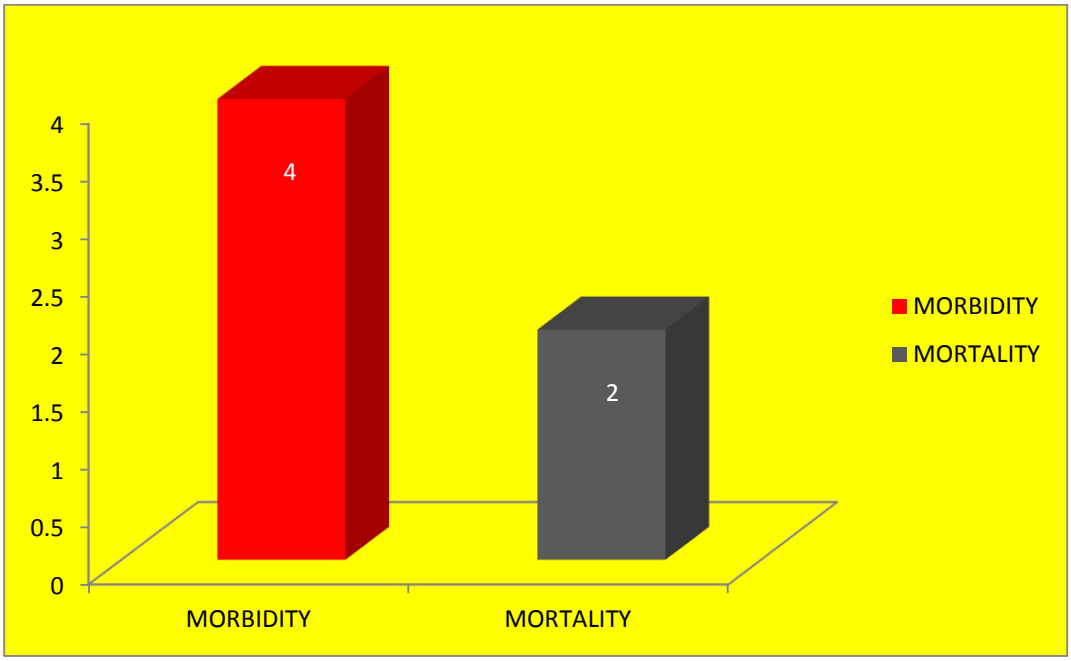

Figure 4: Association of native treatment and outcome

The people who went some form of traditional or unauthorized method of treatment show increased morbidity (20%) and mortality (10%) than who don't.

Tab 2.3: Identification of snakes

Snake identified	No of patients	Percentage
YES	184	46%
NO	219	54%

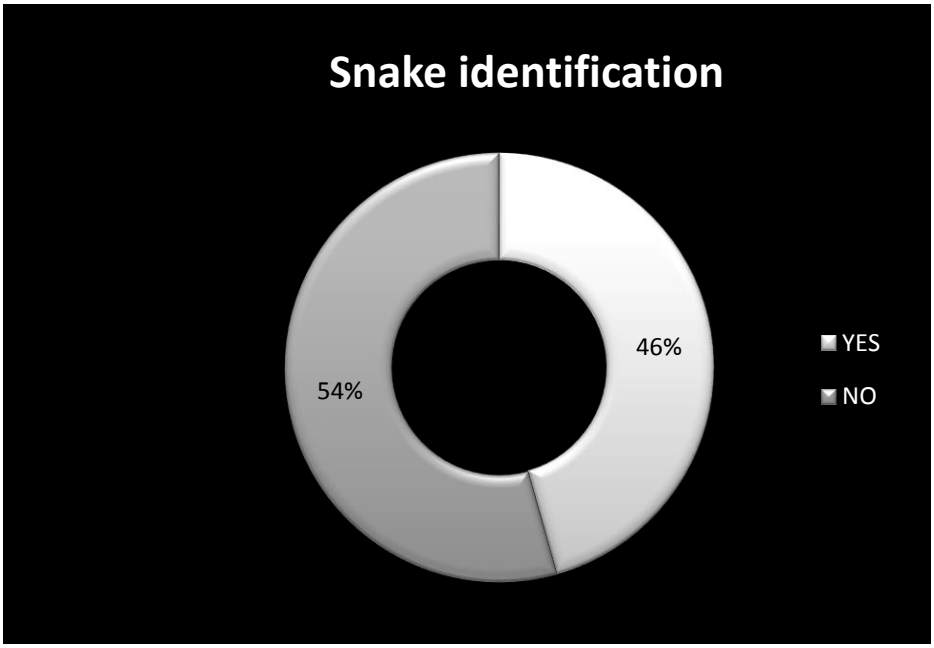

Figure 5: Identifcation of snakes

The snake was correctly identified either with history of with the help of photographs is in only 46% of the patients. In remaining the identification was not possible.

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Tab 2.4 :Type of snakes

TYPE OF SNAKE	No of patients	Percentage
COBRA	42	23.00%
RUSSELS	68	37%
SAW SCALED	55	30%
KRAIT	19	10%

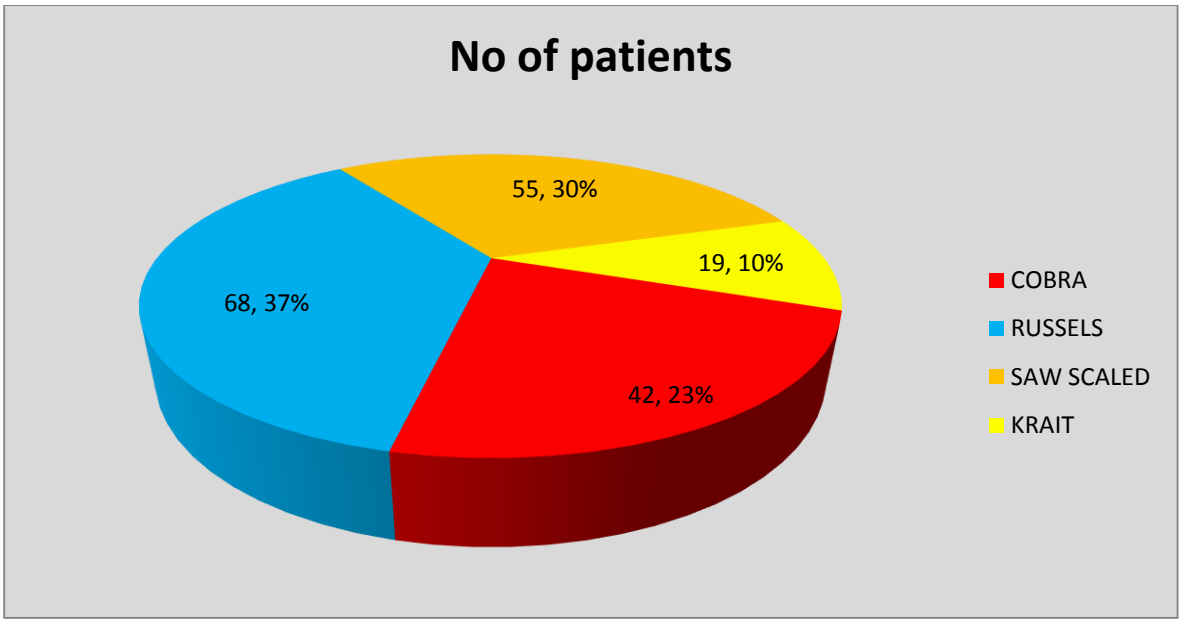


Figure 6: Snake identification

In more than half of the patients snakes was not identified. Among the identified snakes Russell's viper is the most common snake type accounts for 23% of the cases and least common is Krait 10%.

TABLE 3: PRESENTING SYMPTOMS

Symptoms	No	Yes	%
Pain and Swelling	243	160	39%
Bleeding	380	23	5.7%
Muscle Weakness	361	42	10.4%
GI symptoms	393	10	2.4%
Breathlessness	369	34	8.4%

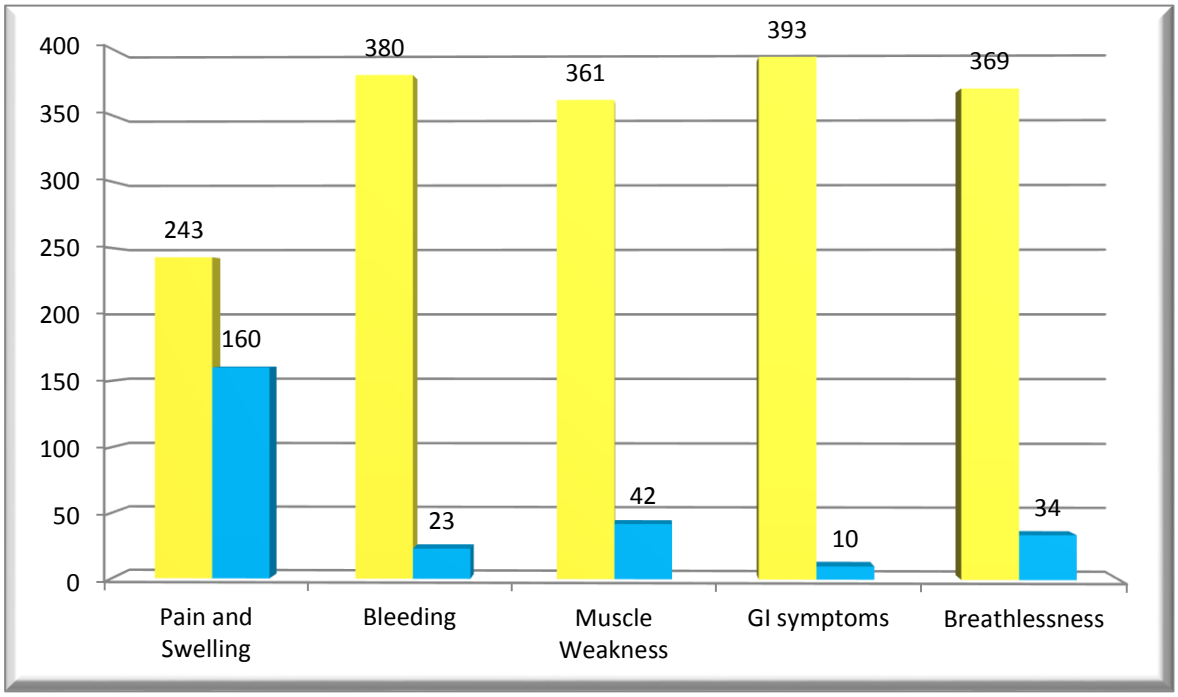


Figure 7: Presenting complaints of the patients

The most common presenting complaints in our study is that of pain and swelling at the bite site and least common is the Gastrointestinal symptoms (such as vomiting, abdominal pain).

TABLE 4: AUTONOMIC HYPERACTIVITY

Autonomic hyperactivity	No	Yes	%
hyperglycemia	379	24	5.9%
hypertension	390	13	3.2%
sweating	359	44	10.9%
Tachycardia	340	63	15.6%

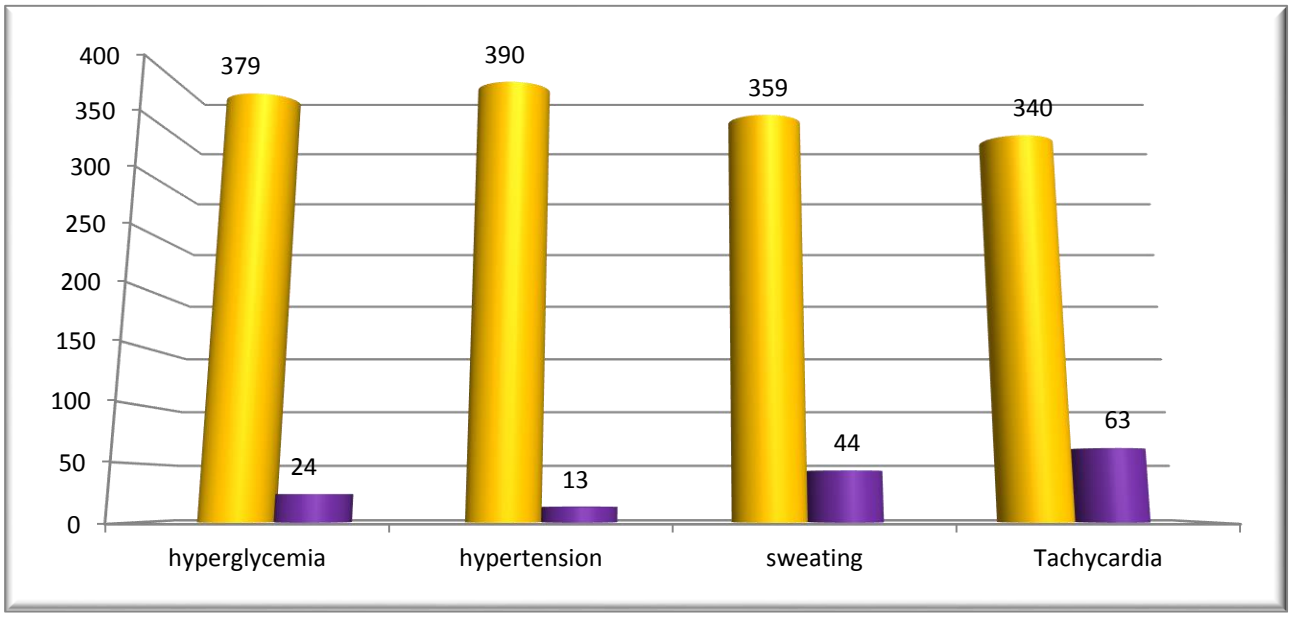
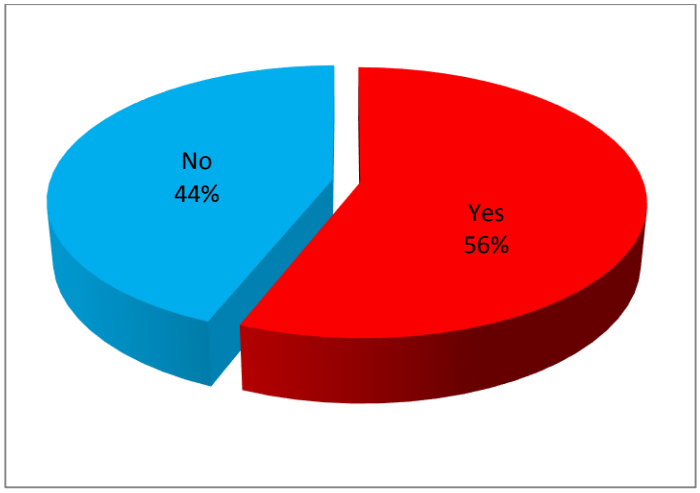


Figure 8: Signs of autonomic hyperacitivity

Out of all patients presented with snake bite only few shows the signs of autonomic hyperactivity . Among the most common manifestation was the tachycardia (15.6%) followed by sweating and palpitation (10.9%). Hyperglycemia and hypertension was also not in few.

TABLE 5: SIGNS OF ENVENOMATION



	Signs of envenomation	Percentage (%)
Yes	226	56%
No	177	44%

Figure 9: Signs of Envenomation

Out of 403 snake bite patients studied only 226 (56%) patients showed the sign of envenomation , 177 (44%) patients showed no evidence of envenomation.

Figure 10: Signs of envenomation

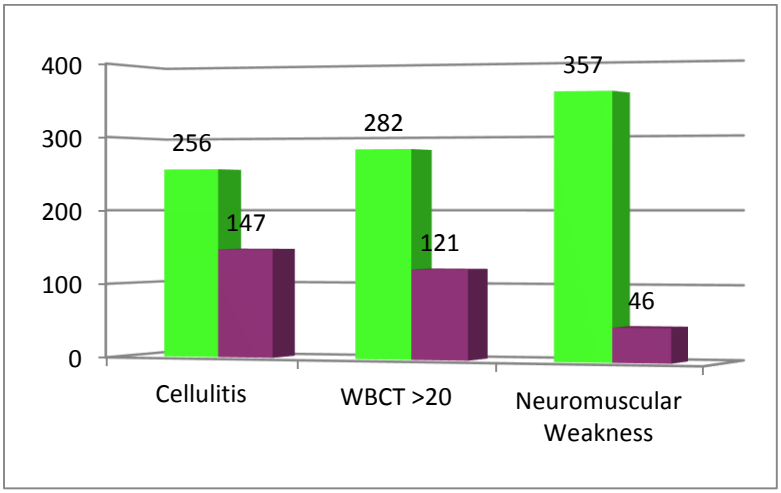


TABLE 6: ENVENOMATION SIGNS

SIGNS OF ENVENOMATION	Yes	No	%
Cellulitis	147	256	36.4%
WBCT >20	121	282	30%
Neuromuscular Weakness	46	357	11.4%

Among 226 patients who showed the signs of envenomation cellulitis is the major sign followed by the prolonged clotting time and the last is the neuromuscular weakness.

Table 7: Comorbidities in the study group

Comorbidities	No	Yes	%
Diabetes	366	37	9.1%
Hypertension	373	30	7.4%
PTB	401	2	0.4%
Asthma	395	8	1.9%
CAD	379	24	5.9%

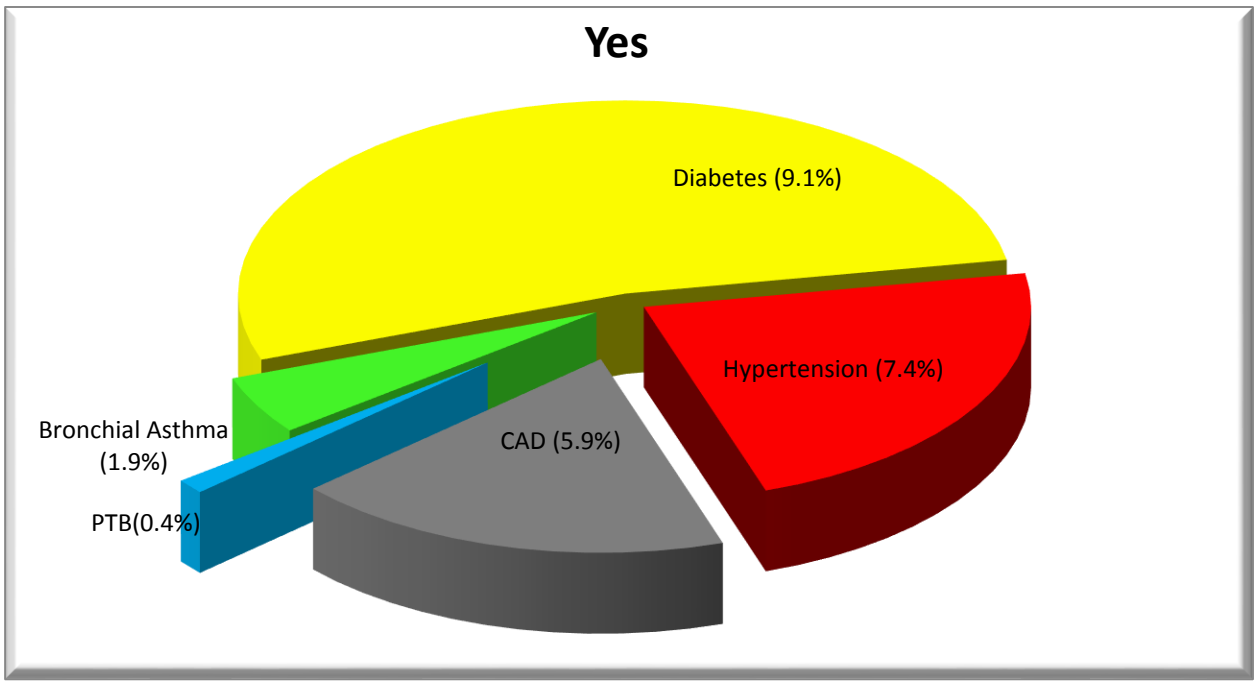


Figure 11: Comorbidit ies

Among the study patients around 9 % were diabetic and 7.4% were hypertensive. 2 patients gave the history PTB in the past and 8 people had bronchial asthma (mild) who used intermittent inhaler therapy.

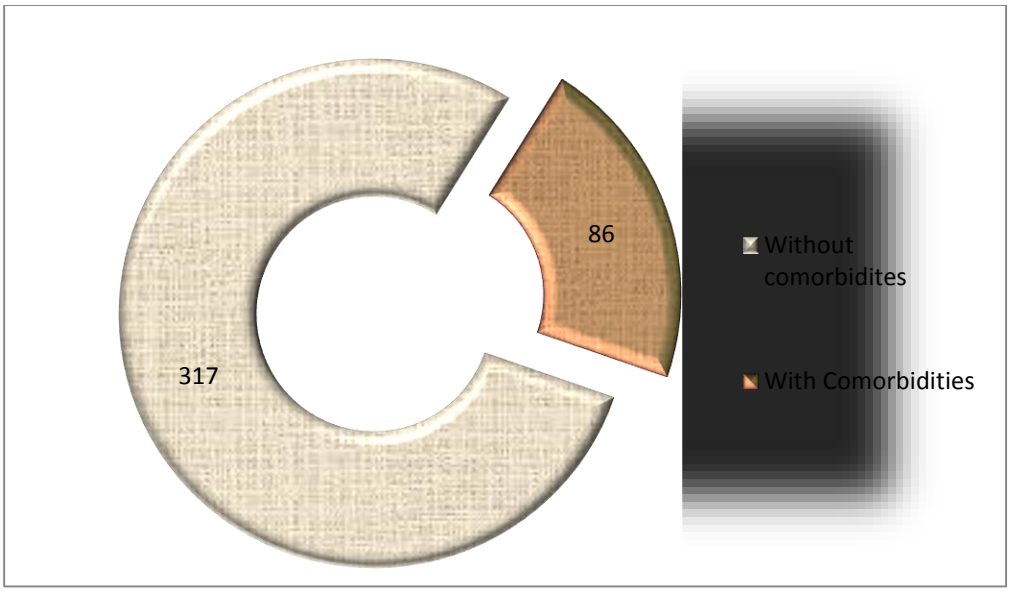


Figure 12: Comorbities

In our study population of 403 patients 86 patients (21%) had comorbid conditions. The contribution of these comorbidities in the outcome of the patients had been considered in the studies.

COMPLICATIONS:

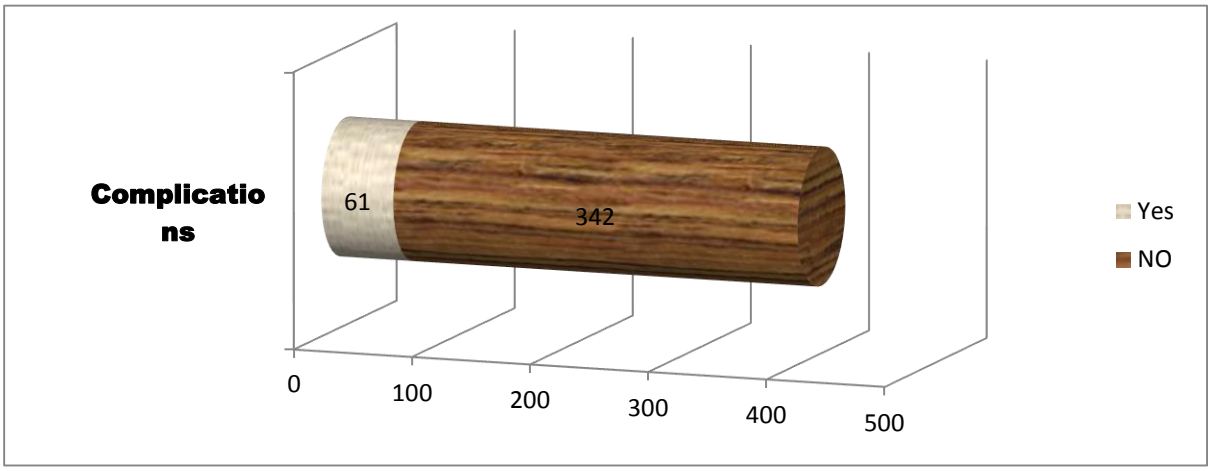


Figure 13: Complications of snake bite

Among the 403 patients without snake bite 61(15.1%) developed one or more complications.

TABLE 8: COMPLICATIONS OF SNAKE BITE

Complications	No	Yes	Percentage (%)
AKI	376	27	6.6%
compartment syndrome	367	36	8.9%
DIC	394	9	2.2%
Respiratory failure	379	24	5.9%
Sepsis	380	23	5.7%

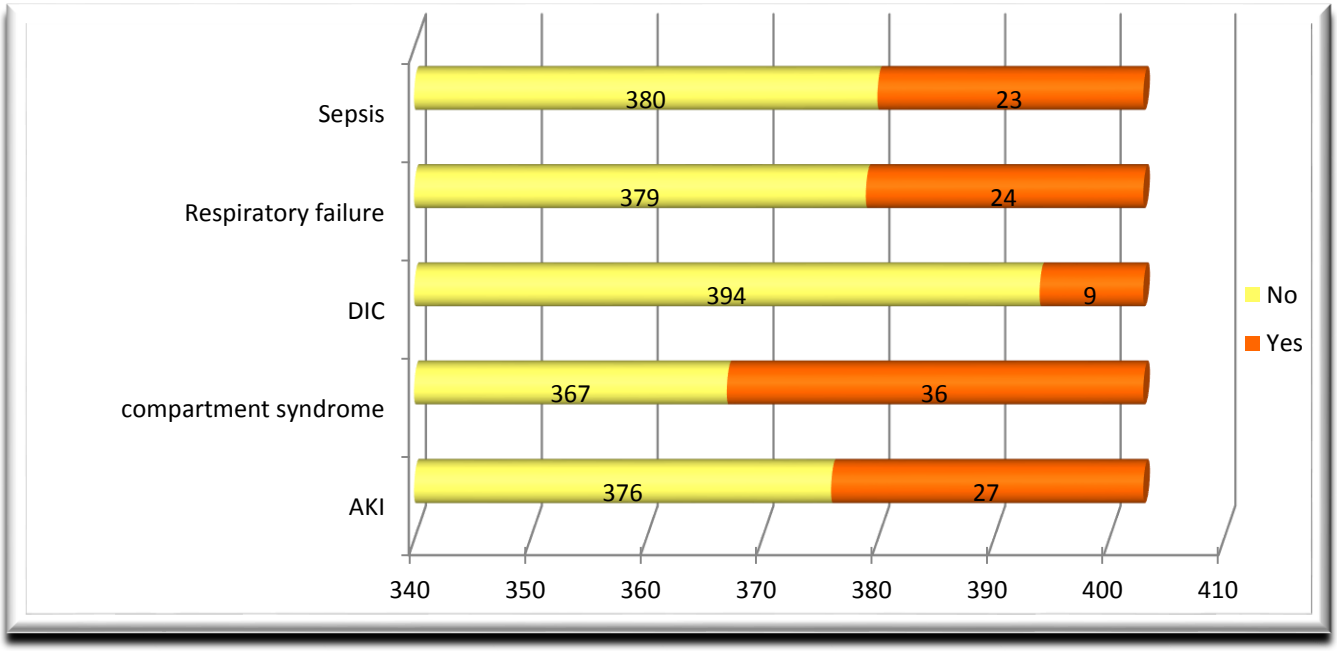


Figure 14 : Compliactions of Snake bite

Compartment syndrome (8.9%) is the most frequent complication encountered in the study population. DIC(2.2%) is the least common complication observed in the study group.

TABLE 9: NUMBER OF COMPLICATIONS

Number of complications	Frequency	Percentage(%)
No	342	84.8%
1.00	41	10.1%
2.00	11	2.7%
3.00	8	1.9%
4.00	1	0.2%

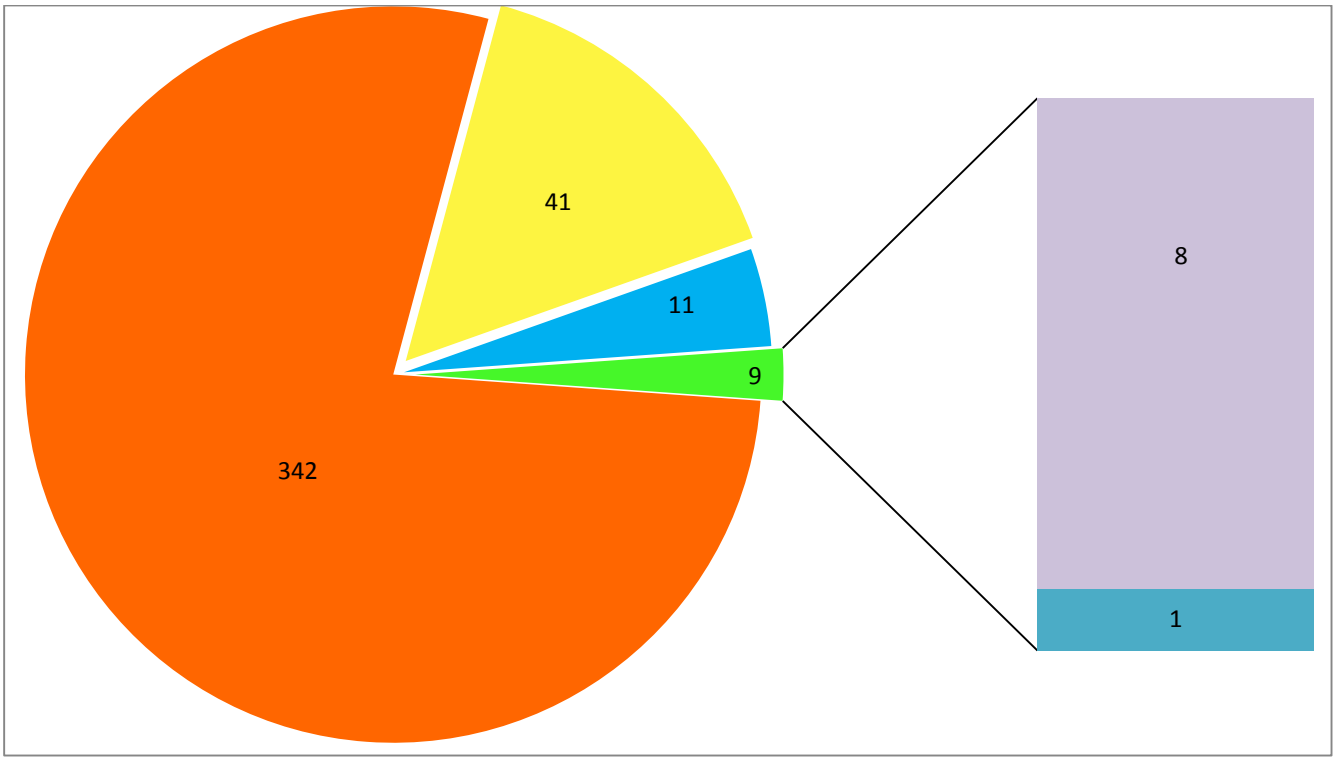


Figure 15: No of Complications

Among 61(15.1%) who developed complications 41 patients0(10.1%) had single complication , 11 patients(2.7%) had 2 complications,8 patients (1.9%) 2 complications and 1 had 4 complications.

TABLE 10: OUTCOME

OUTCOME	No	Yes	Percentage (%)
Completely recovered	44	359	89%
Disabilities	370	33	8.1%
Death	392	11	2.7%

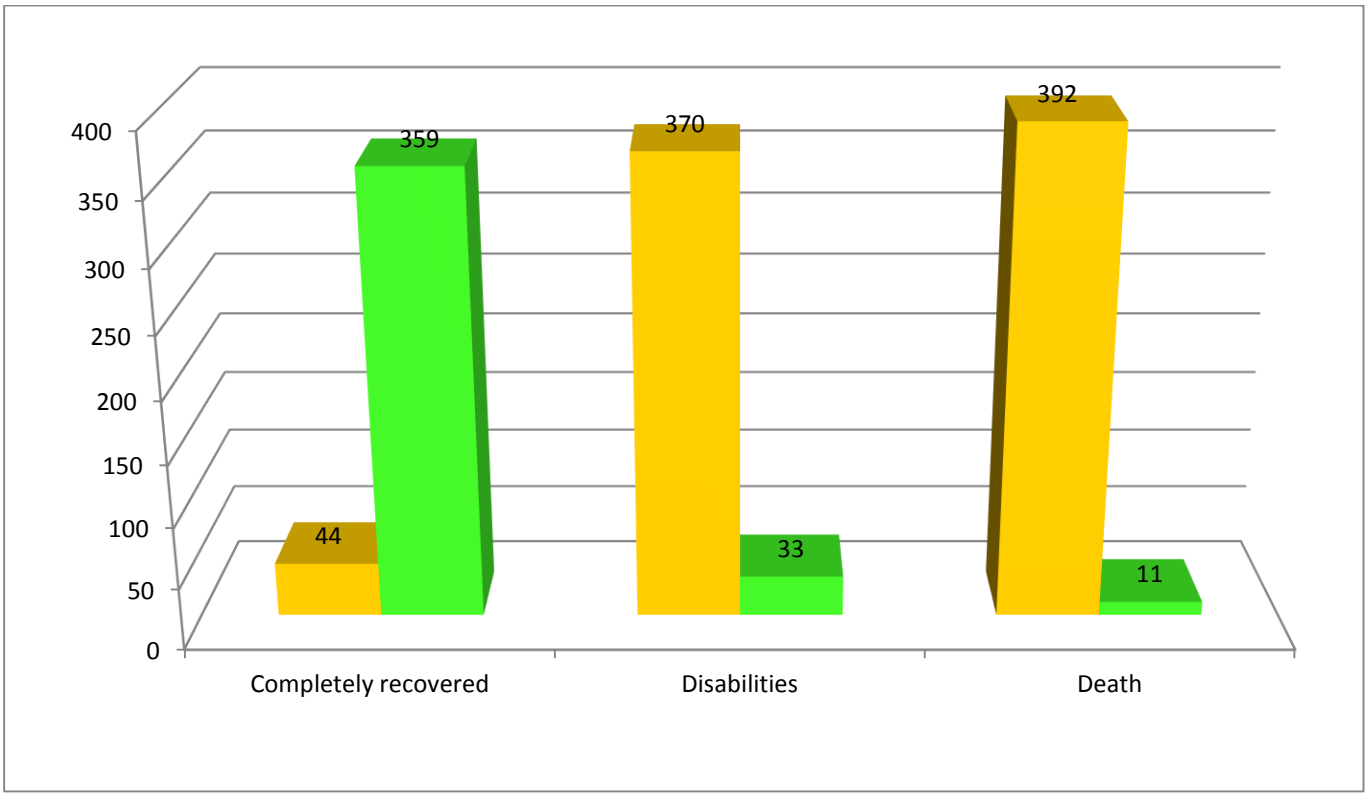


Figure 16: Outcome of the patients with snake bite

Overall outcome was good for the patients admitted with snake bite. 359 (89%) patients recovered completely following snake bite , 33 patients had morbidity and 11 patients expired due to complications of snake bite.

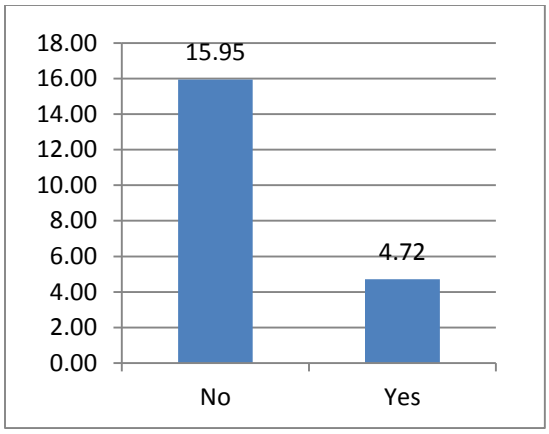


Figure 17.1: Complete recovery based on time lag

Table 11.1: Complete recovery based on time of seeking medical care

Complete Recovery		N	Mean	Std. Deviation	P value
Time lag between bite and seekng medical care	No	44	15.95	18.46	<0.0001
	Yes	358	4.72	3.79	

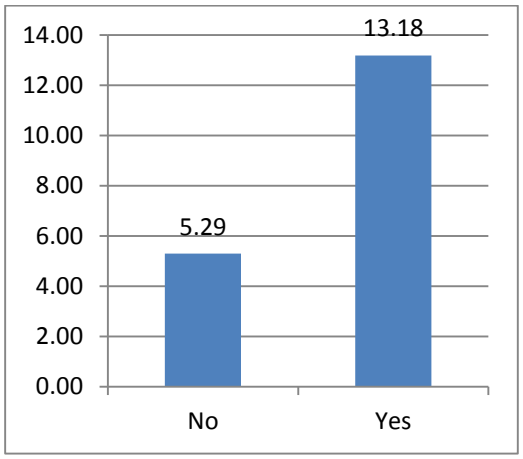


Figure 13.2: Disabilities based on time lag

Table 11.2: Morbidity based on time of seeking medical care.

Disabilities		N	Mean	Std. Deviation	P value
Time lag between bite and seekng medical care	No	370	5.29	5.71	<0.0001
	Yes	33	13.18	18.37	

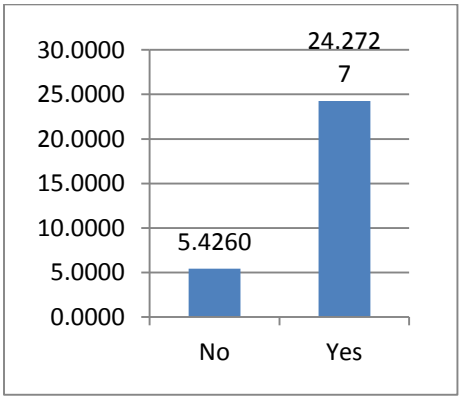


Figure 18: Death based on time lag

Table 11.3: Deaths based on time of seeking medical care.

Death		N	Mean	Std. Deviation	P value
Time lag between bite and seekng medical care	No	392	5.4260	6.80339	<0.0001
	Yes	11	24.2727	16.82909	

The patient who presented to the hospital early following the snake bite had good outcome. Delayed presentation resulted in increased morbidity and mortality.

Table 12.1 : Age relate Complete recovery

outcome		N	Mean	Std. Deviation	P value
age	No	44	49.1136	17.19818	0.001
	Yes	358	40.7235	16.18361	

Table 12.2: Age related morbidity

		N	Mean	Std. Deviation	P value
age	No	370	41.0270	16.27572	0.008
	Yes	33	48.9394	17.24083	

Table 12.3 : Age related mortality

Death		N	Mean	Std. Deviation	P value
age	No	392	41.3903	16.45588	0.038
	Yes	11	51.8182	14.53147	

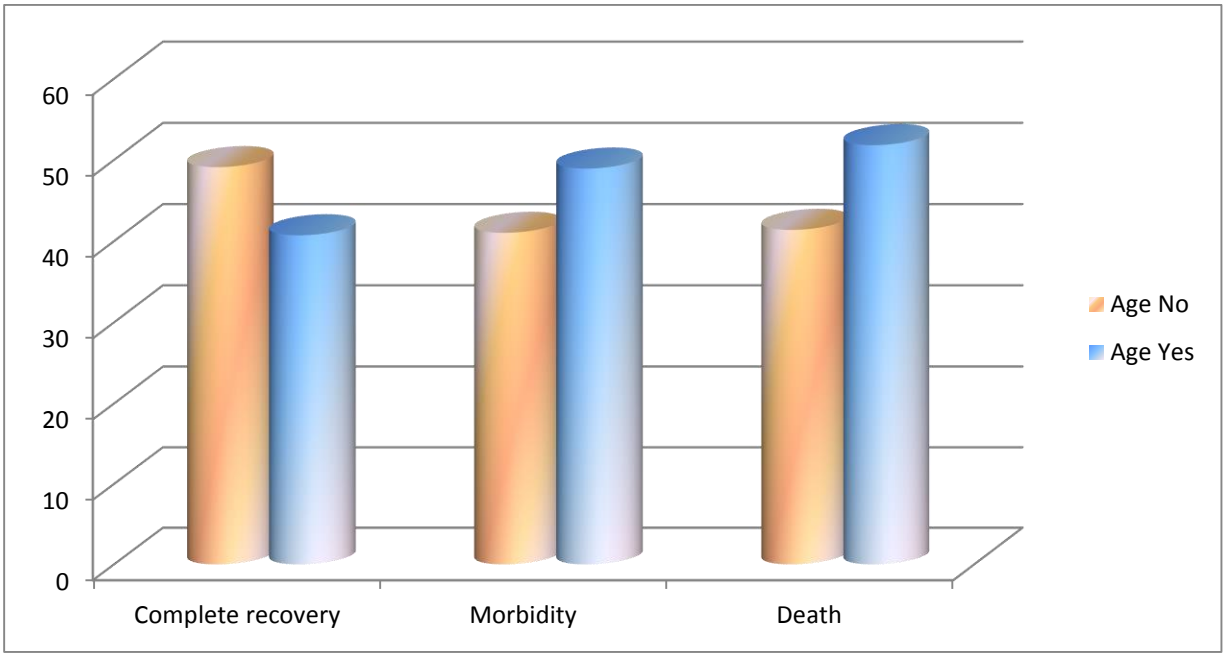


Figure 19: Age related outcome of snake bite patients

According to the study result patients with young age had good recovery. Mean age of <40 have favoruably outcome than the mean age of >40 in the study population.

Table 13: Diabetes Mellitus and the outcome of snake bite patients

Table 13.1: Diabetes mellitus related complete recovery

		complete Recovery		Total	P value
		No	Yes		
Diabetes	No	30	336	366	<0.0001
	Yes	14	23	37	
Total		44	359	403	

Table 13.2 : Diabetes and Disabilities

		Disabilities		Total	P value
		No	Yes		
Diabetes	No	343	23	366	<0.0001
	Yes	27	10	37	
Total		370	33	403	

Table 13.3: Diabetes and Death

		Death		Total	P value
		No	Yes		
Diabetes	No	359	7	366	0.002
	Yes	33	4	37	
Total		392	11	403	

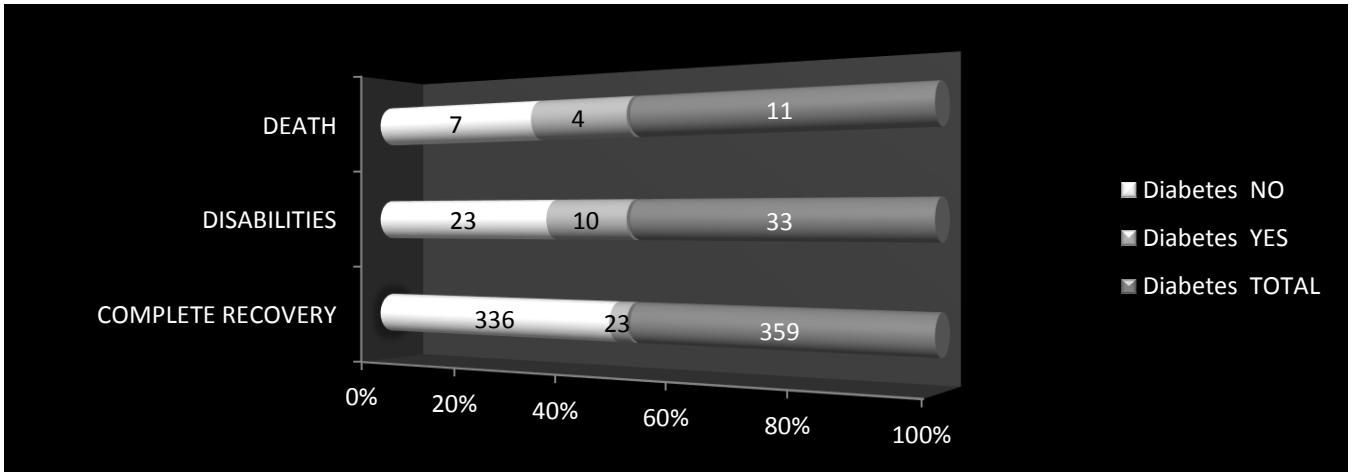


Figure 20: Diabetes related outcomes

Diabetes is one of the factor play a pivotal role in the outcome of the patients. Around 50% patients who had morbidity and mortality had Diabetes.

		Complete Recovery		Total	P value
		No	Yes		
DIC	No	37	357	394	<0.0001
	Yes	7	2	9	
Total		44	359	403	

Table 15.2: DIC and morbidity

		Morbidity		Total	P value
		No	Yes		
DIC	No	362	32	375	0.356
	Yes	8	1	9	
Total		370	33	403	

Table 15.3: DIC and mortality

		Mortality		Total	P value
		No	Yes		
DIC	No	370	5	375	<0.0001
	Yes	2	6	9	
Total		392	11	403	

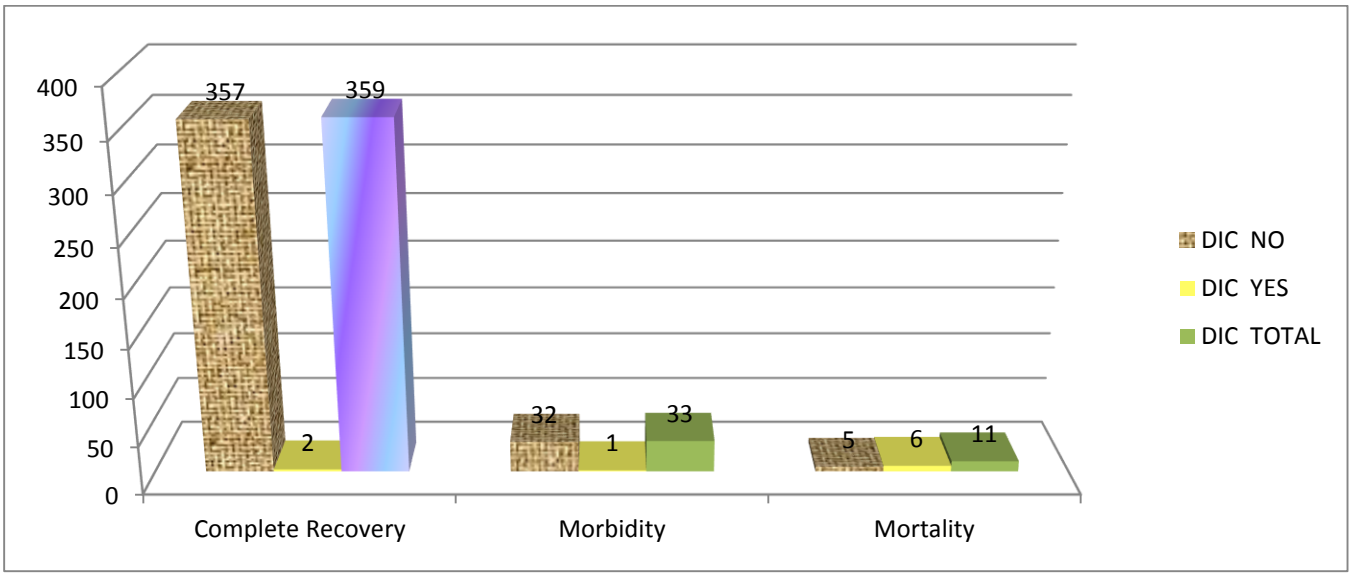


Figure 21: DIC related outcome

DIC increases the riskof mortality significantly in patients with snake bite but if treated properly doesn't produce any morbidity and recovery is complete.

Table 16: Correlation between Neuromuscular weakness and Respiratory failure

		Respiratory failure		Total	P value
		No	Yes		
Neuromuscular weakness	No	351	6	357	<0.0001
	Yes	28	18	46	
Total		379	24	403	

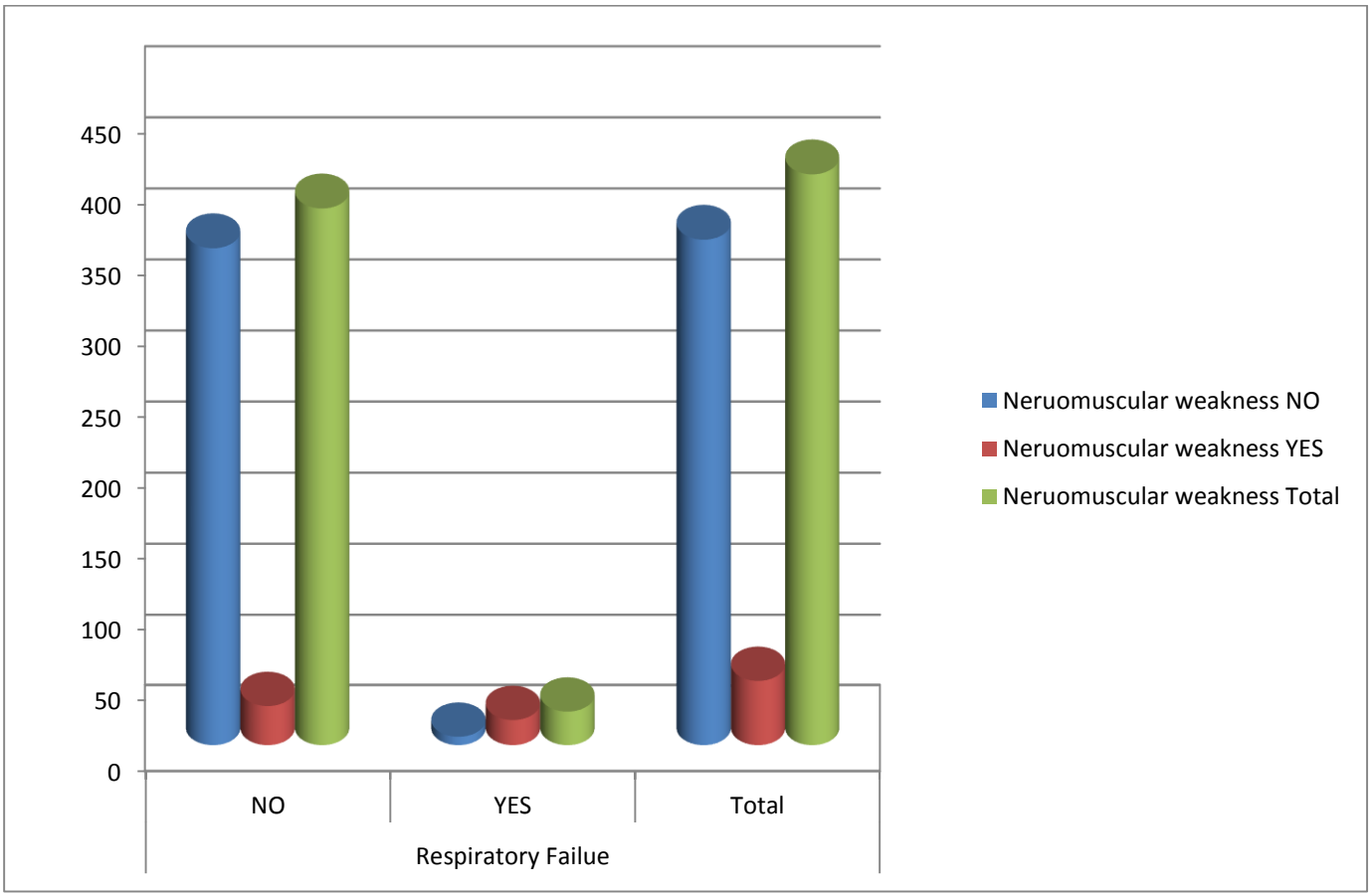


Figure 22: : Correlation between Neuromuscular weakness and Respiratory failure

According to our study all the patients who developed respiratory failure showed some kind of neuromuscular weakness. Some patients who showed muscular weakness didn't developed respiratory failure because of the treatment given.

Table 17: Cellulitis based Outcomes

Table 17.1: Cellulitis and complete recovery correlation

		outcome		Total	P value
		No	Yes		
cellulitis	No	6	250	256	<0.0001
	Yes	38	109	147	
Total		44	359	403	

Table 17.2: cellulitis and morbidity correlation

		Morbidity		Total	P value
		Yes	No		
cellulitis	No	4	250	256	<0.0001
	Yes	29	109	147	
Total		33	370	403	

Table 17.3: cellulitis and mortality correlation

		Death		Total	P value
		No	Yes		
cellulitis	No	256	0	256	<0.0001
	Yes	136	11	147	
Total		392	11	403	

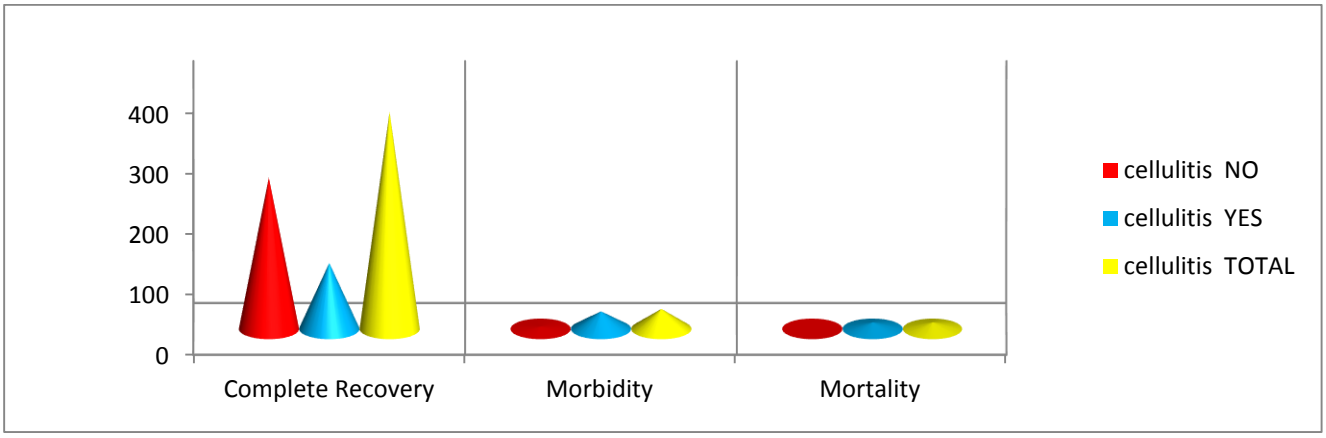


Figure 23: Cellulitis and outcome correlation

All the patient who died had cellulitis. Cellulitis increased the morbidity significantly. 29 out of 33 patients who had morbidiy had cellulitis. Cellulitis is one of the major factor which significantly prolonged the hospital stay in snake bite patients.

Table 18: WBCT and clinical Outcome

Table 18.1: WBCT and complete recovery correlation

		Complete_recovery		Total	P value
		No	Yes		
WBCT	<20	30	252	282	0.783
	>20	14	107	121	
Total		44	359	403	

Table 18.2: WBCT and morbidity correlation

		discharge_disability		Total	P value
		No	Yes		
WBCT	<20	259	23	282	0.971
	>20	111	10	121	
Total		370	33	403	

Table 18.3: WBCT and Mortality correlation

		death		Total	P value
		No	Yes		
WBCT	<20	275	7	282	0.642
	>20	117	4	121	
Total		392	11	403	

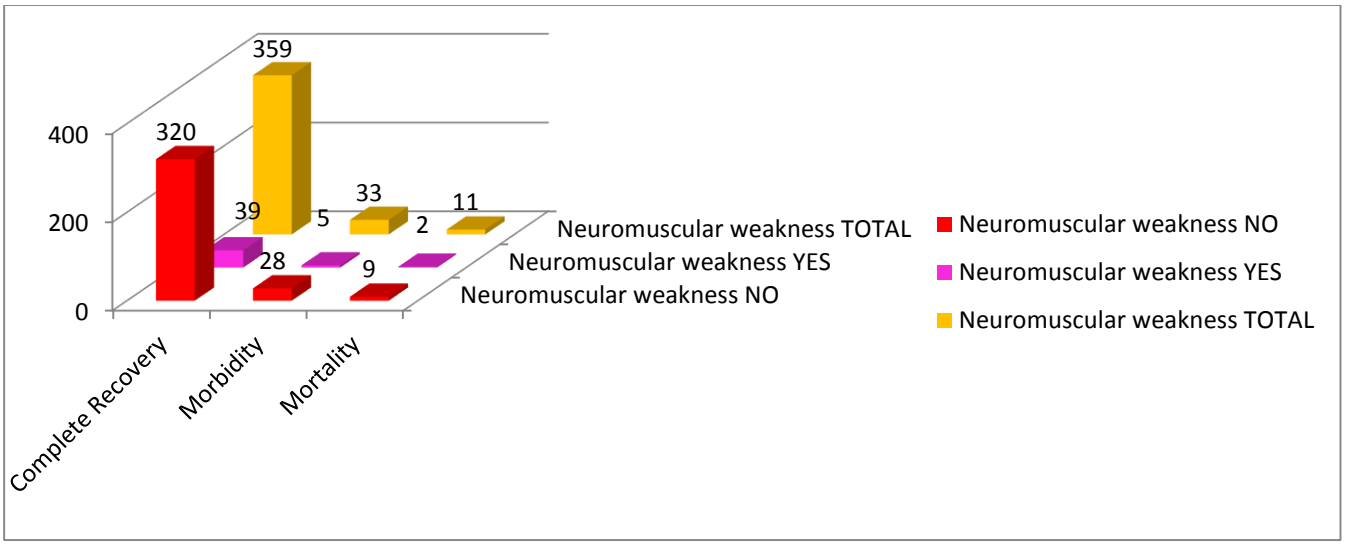


Figure 24: WBCT and outcome correlation

WBCT not significantly affect the outcome of the patients. It signifies the risk of development of DIC but much of the abnormality corrected by administration of ASV. Patients outcome did not greatly varied between those who have prolonged clotting time from those who have normal clotting time.

Table 19: Neuromuscular weakness and Clinical outcome correlation

Table 19.1: Neuromuscualr weakness and complete recovery correlation

		Complete Recovery		Total	P value
		No	Yes		
Neuromuscular weakness	No	37	320	357	0.321
	Yes	7	39	46	
Total		44	359	403	

Table 19.2: Neuromuscualr weakness and morbidity correlation

		Morbidity		Total	P value
		No	Yes		
Neuromscular weakness	No	329	28	357	0.481
	Yes	41	5	46	
Total		370	33	403	

Table 19.3: Neuromuscualr weakness and mortality correlation

		Death		Total	P value
		No	Yes		
Neuromuscular weakness	No	348	9	357	0.474
	Yes	44	2	46	
Total		392	11	403	

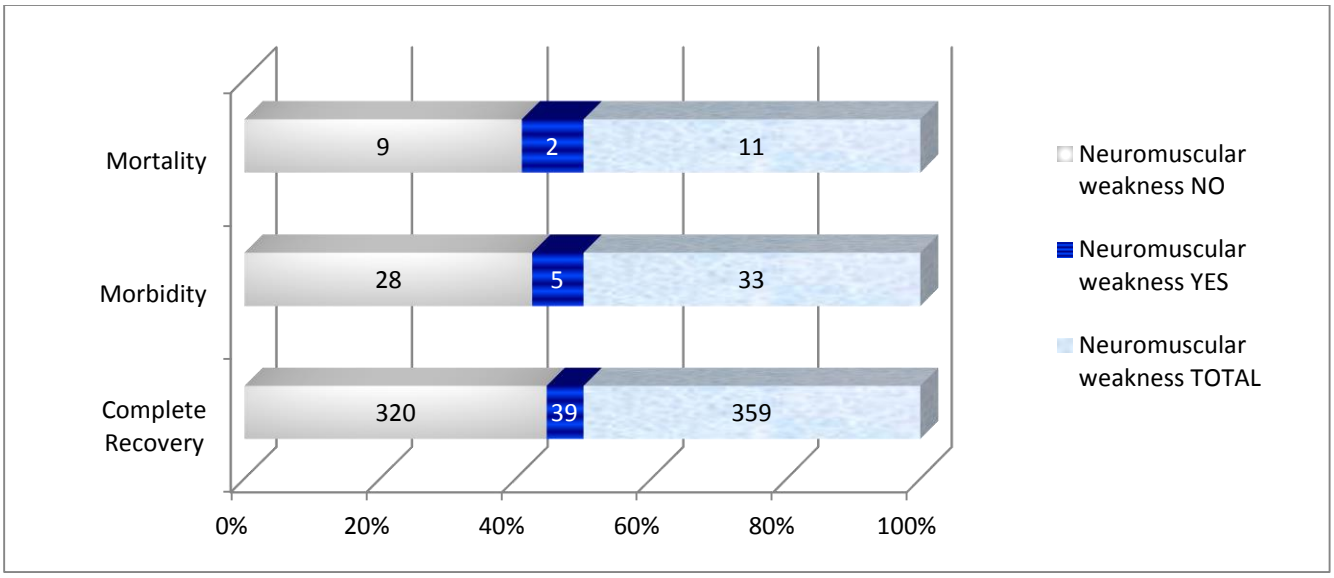


Figure 25: Neuromuscular weakness and outcome correlation

Although neuromuscular weakness leads to respiratory failure and need for ventilatory support subsequently increased, the outcome is not significantly affected. Out of 46 presented with weakness 39 recoverd completely, only 5 developed some kind of morbidity and death occurred in 2 of the patients.

TABLE 20: SEPSIS AND MORTALITY CORREALTION

		Death		Total	P value
		No	Yes		
Sepsis	No	379	1	380	<0.0001
	Yes	13	10	23	
Total		392	11	403	

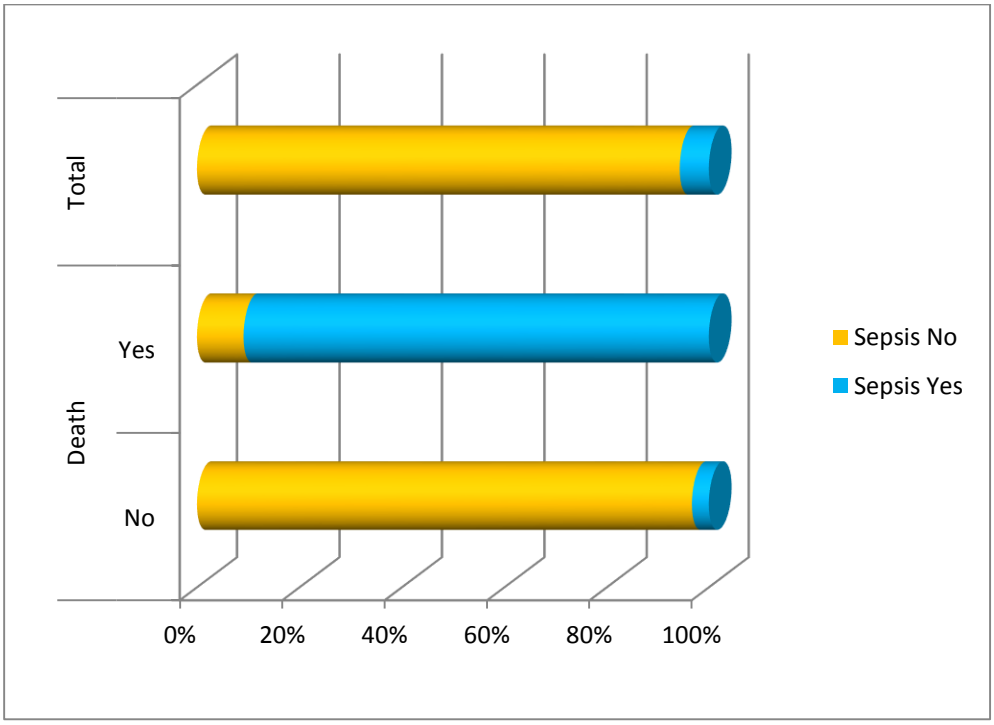


Figure 26: Sepsis and outcome correlation

Sepsis is the major complication which increased the mortality of the patients. Among 11 people who died 10 developed sepsis. Early treatment of sepsis can prevent mortality.

Month	January	February	March	April	May	June	July	August	September	October	November	December
No of cases	31	20	38	40	49	42	36	34	24	26	30	33

Table 21: MONTHLY DISTRIBUTION OF SNAKE BITE CASES

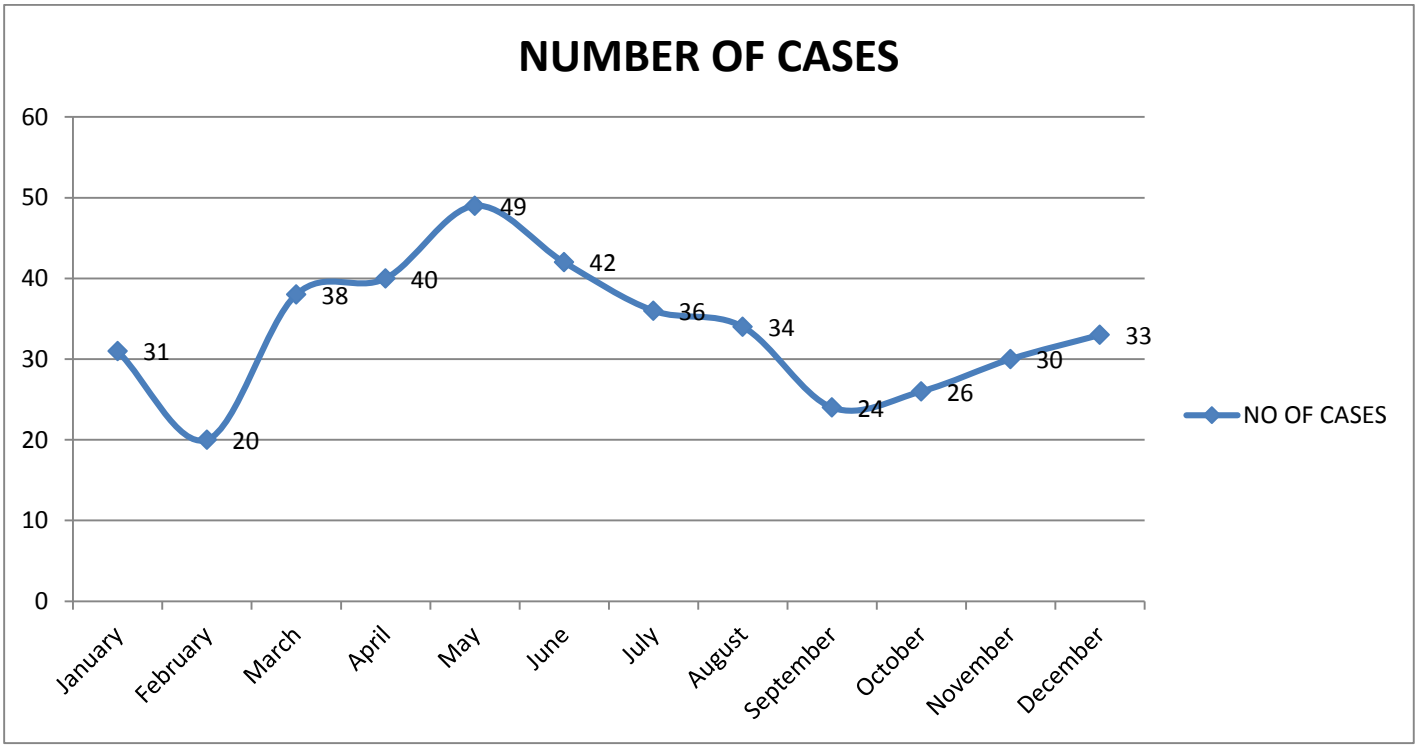


Figure 27: Monthly Distribution of cases

The no of snake bite cases admitted in Tirunelveli medical college is maximum at mid year period. May month has the maximum no of cases (49) and February month had the least no of cases (20) followed by September (24).

TABLE 22 : OUTCOME BASED ON NUMBER OF COMPLICATIONS

Table 22.1: Complete Recovery based on number of complications

		Complete_recovery		Total	P value
		No	Yes		
No of complications	No	3	306	309	<0.0001
	1.00	23	45	68	
	2.00	10	7	17	
	3.00	7	1	8	
	4.00	1	0	1	
Total		44	359	403	

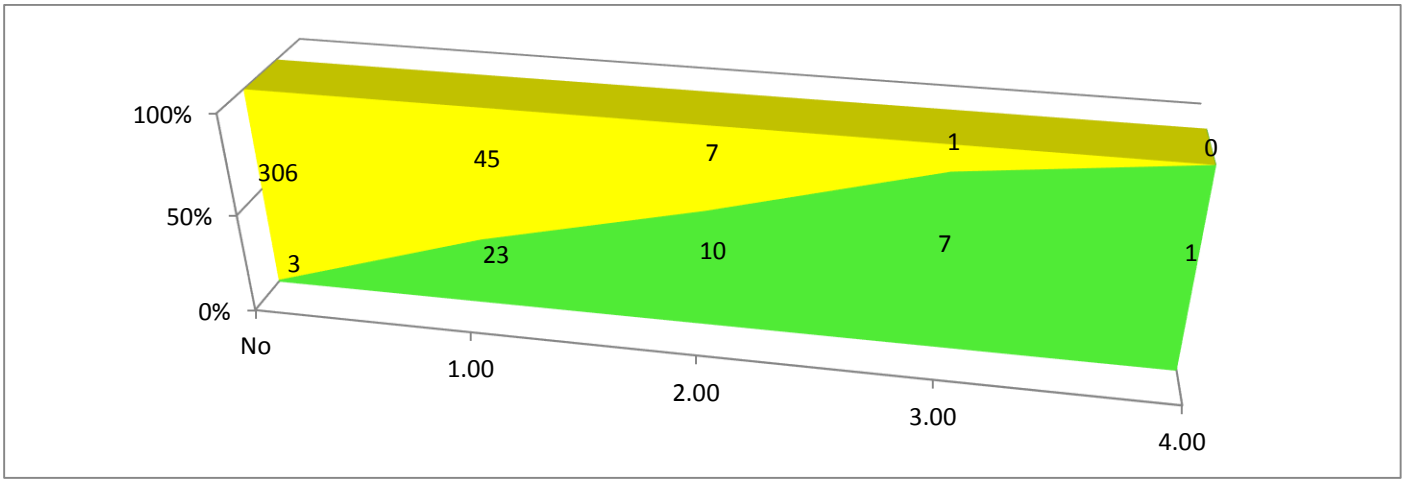


Figure 28: Complete recovery based on number of complications

Those who had less number of complications had good clinical recovery than those had more complications.

Table 22.2: Morbidity based on number of complications

		Morbidity		Total	P value
		No	Yes		
No of complications	No	307	2	309	<0.0001
	1.00	45	23	68	
	2.00	10	7	17	
	3.00	7	1	8	
	4.00	1	0	1	
Total		370	33	403	

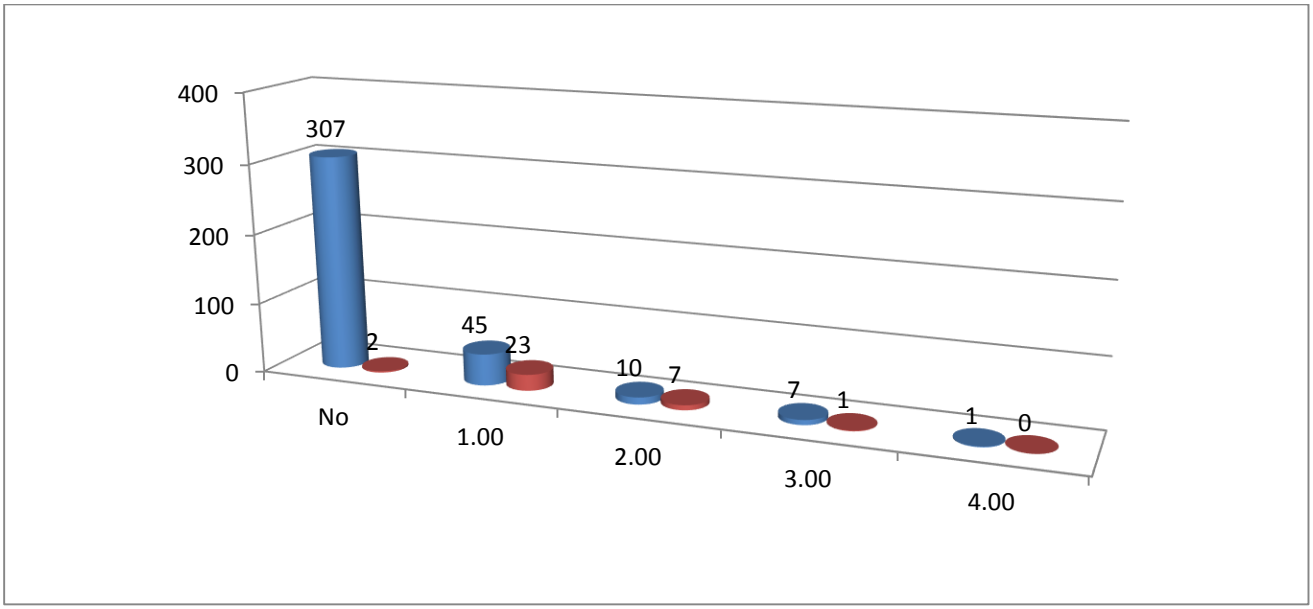


Figure 29: Morbidity based on number of complications.

The number of morbidity also increased proportionately with increased numberof compliacations.

Table 22.3: Mortality based on number of complications

		Death		Total	P value
		No	Yes		
No of complications	No	309	0	309	<0.0001
	1.00	67	1	68	
	2.00	14	3	17	
	3.00	2	6	8	
	4.00	0	1	1	
Total		392	11	403	

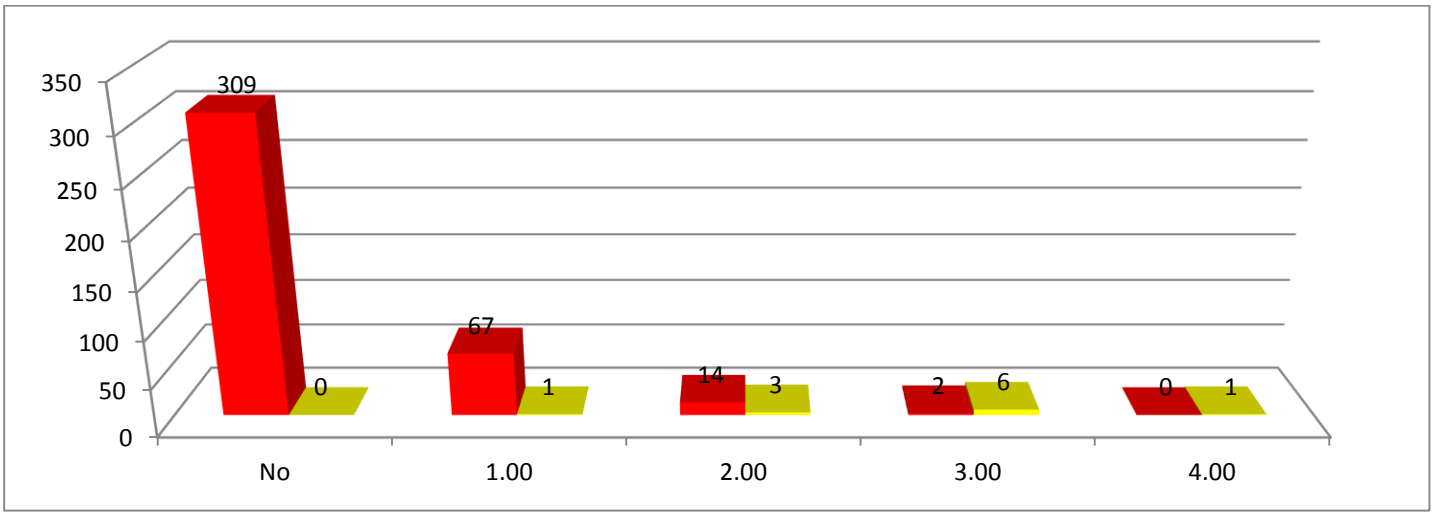


Figure 30: Mortality based on number of complications

The number of deaths increases with increasing complications. Among 68 people with single complication one died but the number increases with 3/17 for 2 complications, 6/8 for 3 and 1/1 for patient who developed 4 complications.

DISCUSSION

In this study, all the 403 patients admitted in Tirunelveli medical college hospital for the period of one year (from 1st May 2017 to 30th April 2018) with the definite history of snake bite were studied since the admission till the final end point (Discharge /Death). Among the all the patients studied, the incidence of snake bite is more common among men (65%) than women (35%). This comparable to study conducted by *Nandita, Agarwal et al(2018)*[5] where the males are the majority affected. The 95.30% bites were occurred when the patients were outside their home (384 patients) and bites were common in rural areas and among the farmers and agricultural laborers. Other activities which are having increases risk of exposure the snake bites are collecting longs, gardening and playing or working near the bushy areas. This is the similar case mentioned in the article *Myint-Lwin, Warrell DA, Phillips RE, et al*.

19 patients (4.7%) who had their bite inside their home were in their sleep and snake was not identified in the majority but in some cases the snake was identified and it belongs to the krait variety. This is comparable to *Faiz A, Ghose A, Ahsan F, et al*[15] *; Ariaratnam CA, Sheriff MH, Theakston RD, et al*[16]*; Sharma SK, Chappuis F, Jha N, et al*[17], where the snake responsible for bite during the sleep is krait in India, Sri Lanka, Nepal.

During the one year study period the total number of snake bite patients admitted was 403. This contributed to 1.7% of all the admissions (24,847 patients) in our medicine department. The mortality due to snake bite was 11 in our study period which accounted for 0.6% of overall mortality.

The patients were subjected to predesigned questionnaire (annexure II) on the time of admission and outcome of patients based on the number of factors assessed. The practice of unauthorized mode of treatment was present in 20 patients (5%) and the most common method is application of tourniquet above the bitten area, followed by incision with sharp objects at the bite site. The morbidity (4 pts) and mortality (2 pts) showed significantly high in patients underwent treatment by other means, this is partly because of unwanted delay occurs before seeking medical care and administering ASV. It is also due to manipulation at the bite site increases the risk of secondary bacterial infection producing significant sepsis and related complications and decreased blood supply due to tight application of tourniquet aggravates the local effects of envenomationa and favours necrosis. This is also mentioned in the *Tun Pe, Tin-Nu-swe, Myint=l.win, warreil DA, Than-win et al*[45], *Guderian RH, Mackenzie CD, Williams JF*[46], *Bush SP Hegewald KG, Green SM, cardwell MD, Hayes wK et al* [47].

The incidence of morbidity is in rise when the age of the patient increases. The mean age of 40 and below are having favorable outcome than the patients with

mean age ≥ 48. The mortality also increases with age because of presence of co morbidities which significantly affects the outcome of the patient. This is as same as mentioned in the study *Mohapatra B, Warrell DA, Suraweera W, et al,* where there are 46000 snake bite deaths in India per year accounts for 0.5% of all overall mortality. But in our study the percentage of admission and deaths were compared with our hospital admissions and deaths in our hospital not with the general population.

Among the 403 patients who had the definite snake bite only 220 patients (56%) showed some form of envenomation. 117 patients (44%) showed no symptoms or signs eventhough definitely bitten by snake accounts for "dry bites". Which is comparable *to Warrell DA, Davidson NMcD, Greenwood BM, et al*[21]*; Warrell DA, Davidson NMcD, Greenwood BM, et al* [22].

The bitten snake was identified in only 46% (184 patients) and 54% of patients not identified the snake even with the help of photograph. Since most of the bite was occurred in the evening and night than the day and the location of bite is outdoor mostly in congested areas the identification was not possible in the most of the cases. Among the snakes identified, most of the bites are produced by Vipers, especially Russell's viper accounts for the most of the bites (37%) followed by saw scaled viper (30%). Cobra (23%) and krait (10%) are the most commonly responsible for the neurotoxic snake bites but Russell's viper

also produce some neurotoxicity in 3 patients but not amounting to respiratory failure; *Wüster W, Otsuka S, Malhotra A, Thorpe RS et al*[12],

The most common presenting symptom following snake bite is Pain and swelling at the bite site accounts for 39% of cases and least common is GI symptoms (2.4%). Some patients showed signs of autonomic arousal on arrival to hospital and the most common sign is tachycardia presented in 15.6% of patients. 5.9% (24) patients had hyperglycemia on arrival which disappeared on follow up period and their HbA1c showed no significant abnormality.

Among our study patients 37 were diabetic which has significant correlation with the outcome of the patient. Mortality and morbidity among diabetic patients were significant with p value of <0.001. Other comorbidities like hypertension and CAD doesn't affect the outcome of the patients significantly; *Sharma SK, Chappuis F, Jha N, et al*[17].

Among the 403 the patients studied 121 patients showed coagulation abnormalities, 159 showed signs of local envenomation and 42 patients showed neurotoxicity. But not all who showed showed coagulation abnormality developed life threatening bleeding it was present in only 9 patients; *Sano-Martins IS, Fan HW, Castro SC, et al*[28]. Like wise among 46 patients, those who showed some form of neurotoxicity only 28 developed respiratory failure. Other

patients improved after administration of ASV and Anticholinestrase. *Agrawal PN, Aqqarawal AN, Gupta D, Behera D, Prabhakar S, Jindal SK*[43]

The most common complication following snake bite is cellulitis and compartment syndrome (8.9%) leading to fasciotomy increases the morbidity and mortality significantly with p value of <0.0001. The patients who had more than one complication had worst prognosis than the patients with single complication alone as mentioned in table 22.1.

The overall outcome was good , 359 patients out of 403 recovered completely without any disabilities, 33 patients developed complications and underwent some invasive procedures or recurrent blood products transfusion and discharged with some disabilities like tracheostomy tube, raw area leg etc. 11 patients were died in the hospital because of multiple complications. Eventhough the mortality is less compared to death of other causes it remains the important health related issue which could be prevented by proper health education of population and avoiding unwanted delay in seeking medical care following snake bite.

CONCLUSION

- The snake bite cases accounts for 1.7% of all admissions in Medicine department in Tirunelveli medical college and hospital (403/24847admissions)

- Signs of envenomation were present in 56% patients. 44% bites accounts for the “dry bites”.

- The most common sign of envenomation was cellulitis (36.4%), coagulopathy as evidenced by WBCT >20 mins (30%) and least common is neurotoxic signs (11.4%)

- Snake was identified in only 46% of the patients. The most common is Russell’s viper (37%), saw scaled viper (30%), Cobra (23%), kraits (10%).

- 21% patients developed complications following snake bite. The most common is compartment syndrome (8.9%), AKI (6.6%), Sepsis (5.7%),Respiratory failure (5.9%),DIC (2.2%).

- Autonomic hyperactivity were present in 19.8% patients and the most common is tachycardia (15.6%). Stress induced hyperglycemia was noted in 5.9% patients which recoverd during the stay in hospital.

- The morbidity following snake bite is 8.1% (33 patients). Most of the patients developed morbidity in the form of wide raw area and underwent SSG in the subsequent follow-ups.

- The mortality following snake bite is 11 (2.7% among the snake bite patients) which accounts for 0.6% of overall mortality in medicine department.

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ANNEXURE I-PROFORMA

Name: Age: Sex:

Occupation Residence:

Date and time of admission in TVMCH:

IP no.:Admitting unit:

- Time of snake bite:
- Time of seeking medical care:
- Any delay occurred: yes/ no

  If yes reason:

- Any local treatment given:yes/no

  If yes specify:

- Place of snakebite: indoor/ outdoor

If outdoor specify:

- Snake identified: yes / no *Type of snake:

  Identified on the spot / with the help of photographs

- Initial treatment given at nearby PHC/hospital: yes/ no

  If yes specify:

Clinical history:

H/o vomiting yes/no

H/o pain and swelling at bite site yes/no

H/o any bleeding manifestations yes/no

If yes specify:

H/o drooping of eyelids yes/no

H/o respiratory distress yes/no

H/o muscle weakness/paralysis yes/no

H/o loss of consciousness yes/no

H/o abdominal pain yes/no

H/o double vision yes/no

H/o difficulty in swallowing yes/no

Past history:

- ❖ Any h/o diabetes mellitus/ hypertension/bronchial asthma/epilepsy/ischemic heart disease/Tuberculosis/connective tissue disorders/CVA

If present specify:

- ❖ H/o previous snake bite and ASV administration:

If yes specify:

- ❖ H/o any allergy:
- ❖ H/o any surgery:

Personal history:

- Diet :
- Smoker :
- Alcoholism :
- Drug abuse :

Examination:

Consciousness :

Orientation :

Other general examination (mention significant findings):

BP : mmHg Pulse: /min

RR: /min

CVS :

RS :

Abdomen :

CNS :

INVESTIGATIONS:

- **CBC:**

TC					
DC					
Hb					
PCV					
Platelet					

- **RFT:**

Sugar						
Urea						
Creatinine						
Sodium						
potassium						

Whole blood clotting time: on admission

Coagulation profile:

PT (sec)						
APTT (sec)						
INR						

ECG :

Chest X ray :

Echocardiography (if done):

Pulmonary function test :

(if done in asthmatics)

Treatment:

ASV administered during admission : vials

Total ASV administered : vials

Any reaction to ASV occurred :

If yes treatment given :

Antibiotics used :

Other treatment :

- ventilatory support required: Yes/ no
  If yes duration:

  Mode: weaning:

  Any associated complications:

- fasciotomy required:

  Extent of lesion :

  Complications :

  Pus c/s of wound :

  Recovery :

- patient go for DIC:

  If yes D dimer value :

  Serum fibrinogen level :

  Bleeding time :

  Clotting time :

- blood transfusion required:

  Type of blood product transfused :

  Any transfusion reaction :

  Patient stabilized after transfusion :

- Haemodialysis required:

  No of cycles :

  Any complications :

  Patient status after HD :

- Any atypical presentation: yes/ no

  If yes specify:

- Patient's outcome:

- Patient status on discharge:

Annexure II – Consent Form

நோயாளிகளுக்கு அறிவிப்பு மற்றும் ஒப்புதல் படிவம்
மருத்துவ ஆய்வில் பங்கேற்பதற்கு

ஆய்வு செய்யப்படும் தலைப்பு :
பங்கு பெறுபவரின் பெயர் :
பங்கு பெறுபவரின் வயது :

		புங்கு பெறுவர் இதனை ✓ குறிக்கவும்
1	நான் மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் நான் படித்து புரிந்து கொண்டேன். என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டுள்ளது என அறிந்து கொண்டேன்	☐
2	நான் இவ்வாய்வில் தன்னிச்சையாக தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும், எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.	☐
3	இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன்.	☐
4	இந்த ஆய்வில் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக் கொள்ள மறுக்க மாட்டேன்.	☐
5	இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன், ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ, அல்லது எதிர்பாராத, வழக்கத்திற்கு மாறான நோய்குறி தென்பட்டாலோ உடனே இதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்கிறேன்.	☐

பங்கேற்பவரின் கையொப்பம் / ..... இடம்.....தேதி.....
கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்.....

ஆய்வாளரின் கையொப்பம் / ..... இடம் ..... தேதி.....

ஆய்வாளரின் பெயர்.....

மையம் .....

கல்வியறிவு இல்லாதவற்கு (கைரேகை வைத்தவர்களுக்கு) இது அவசியம் தேவை

சாட்சியின் கையொப்பம் / ..... இடம் ..... தேதி .....

பெயர் மற்றும் விலாசம் .....

INFORMED CONSENT FORM

Study Title _____

Study Number _____

Subject's Full Name _____

Date of Birth/Age _____

Address _____

1. I confirm that I have read and understood the information sheet dated for the above study and have had the opportunity to ask questions.
   OR I have been explained the nature of the study by the Investigator and had the opportunity to ask questions
2. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason and without my medical care or legal rights being affected.
3. I understand that the sponsor of the clinical trial/project, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. However, I understand that my Identity will not be revealed in any information released to third parties or published.
4. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s)
5. I agree to take part in the above study

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative: _____

Signatory's Name _____ Date _____

Signature of the Investigator _____ Date _____

Study Investigator's Name _____

Signature of the Witness _____ Date _____

Name of the Witness

Annexure III -ABBREVAITIONS

WBCT – Whole Blood Clotting Time

DIC – Dissemniated Intravascular Coagulation

Ach - Acetyl Choline

ACE – Angiotensin Converting Enzyme

ACEI - Angiotensin Converting Enzyme Inhibitor

ASV - Anti Snake Venom

DM - Diabetes Mellitus

PTB - Pulmonary Tuberculosis

BA - Bronchial Asthma

COPD - Chronic Obstructive Pulmonary Disease

CAD - Coronary Artery Disease

CKD - Chronic Kidney Disease

AKI - Acute Kidney Injury

DNA - Deoxyribo Nucleic Acid

NAD - Nicotinamide Adenine Dinucleotide

ECG - Electro Cardio Gram

RBC - Red Blood Corpuscle

AV node - Atrio Ventricular node

ATN - Acute Tubular Necrosis

INR - International Normalised Ratio

FDP - Fibrin Degradation Products

ABG - Arterial Blood Gas

EIA - Enzyme Immune Assay

ELIZA - Enzyme Linked Immuno Sorbant Assay

PCR - Polymerase Chain Reaction

CT - Computed Tomograph

MRI - Magnetic Resonance Imaging

USG - Ultrasound

PI - Pressure Immobilisation

ET - Endo Tracheal tube

IM - Intra Muscular

IV - Intra Venous

SC - Subcutaneous

CPR - Cardio Pulmonary Resuscitation

EF - Ejection Fraction

Echo - Echocardiogram